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FACULDADE DE ODONTOLOGIA DE BAURU

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Análise proteômica do fluido crevicular de dentes decíduos que sofreram traumatismo

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Tese apresentada a Faculdade de Odontologia de Bauru da Universidade de São Paulo para obtenção do título de Doutor em Ciências, no Programa Ciências Odontológicas Aplicadas.

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Orientadora: Profª. Drª. Maria Aparecida de Andrade Moreira Machado

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Paula Karine Jorge

ABSTRACT

Proteomic analysis of crevicular fluid of traumatized primary teeth [tese]. Bauru: Faculdade de Odontologia de Bauru, Universidade de São Paulo; 2018.

Traumatic dental injuries (TDI) often happens in early childhood, the examination method is clinical and radiographic. Another methodology that has been used to aid in TDI diagnosis is molecular biology. A fluid that has been studied in molecular biology is gingival crevicular fluid (GCF), which is an appropriate fluid to evaluate the relation between periodontal tissues and pulp, and its compounds will depend on either the health or inflammation level of tissues. Therefore, this study aimed to characterize the proteins/peptides in GCF of primary tooth with different sequelae of TDI to clarify the proteins/peptides functions in order to contribute in the diagnosis of pulp and periodontal conditions. The sample was composed for 8 children with TDI, ranging 4 to 6 years. GCF samples were collected in 4 points of the gingival sulcus of both the 12 traumatized teeth and the 8 primary first molar, divided into 5 groups: Molar group (deciduous first molar), No alteration, Pulp Canal Obliteration (PCO), Repair-Related Resorption (RRR) and Pulp Necrosis (PN). GCF proteins were subjected to liquid chromatography electrospray ionization mass spectrometry for identification and characterization. 436 single proteins/peptides were found in this study. 43 (9.86%) were in No alteration group, 92 (21.10%) in PCO group, 23 (5.28%) in RRR group, 16 (3.67%) in PN group, and finaly, 114 (26.15%) in molar group. All groups revealed the following peptides/proteins functions: immune response, cell degradation and recycling, repair and maintenance, enzymatic process, cell binding, cell signaling, cell differentiation, cell migration, structural components and antioxidant activity. Proteins functions related to the specific groups: molar group played role in homeostasis process. No alteration group, I6L9F6_HUMAN, NEB2_HUMAN, Q5T0H8_HUMAN, H0YJG4_HUMAN are related to nervous tissue, and, TET1_HUMAN to odontoblast differentiation. RRR group, CALX_HUMAN, B8ZZF0_HUMAN are related to senescence, and KMT2D_HUMAN mutation is associated to skeletal deformation. PCO group, CATA_HUMAN is response to hypoxia, fibroblast transformation, and osteoblast differentiation; MTA70_HUMAN is related to stem cell differentiation; ITPR2_HUMAN releases calcium ion into cytosol. Fistula group: Q8TAS6_HUMAN development of neuronal tissue; E9PDR3_HUMAN neurotransmitter release, cell division and death; B4DT36_HUMAN play a role in conducting axon; C9JN07_HUMAN mitotic process; RSF1_HUMAN DNA repair; Q19KS2_HUMAN immune defense. Concluding, TDI of primary tooth profile undergoing different sequelae type was characterized. The proteins of molar group exhibited complete homeostasis. In no alteration group, the proteins play a role in maintaining the nervous tissue. The proteins of PCO group were involved in cell transformation and differentiation to reach canal root obliteration. The

proteins of RRR group revealed a senescence process. In fistula group the proteins play a role to surround the inflammation site.

Keywords: Proteome. Gingival Crevicular Fluid. Tooth injuries. Tooth, Deciduous.

RESUMO

Análise proteômica do Fluído Crevicular de Dentes Decíduos que sofreram traumatismo [tese]. Bauru: Faculdade de Odontologia de Bauru, Universidade de São Paulo; 2014.

O trauma dentário (TD) geralmente ocorre na primeira infância, e os exames para tratamento e acompanhamento são majoritariamente clínico e radiográfico. Outro método auxiliar que tem sido usado para diagnóstico é a biologia molecular. Sendo, o fluido gengival crevicular (FGC) um fluido apropriado para avaliar a relação entre os tecidos periodontais e a polpa, e seus compostos dependerão do nível de saúde ou inflamação dos tecidos. Desta forma, este estudo teve como objetivo caracterizar as proteínas e peptídeos do FGC de dentes decíduos com diferentes sequelas relacionadas ao TD, a fim de auxiliar no diagnóstico da polpa e condição da periodontal. A amostra foi composta por crianças com TD, com a faixa etária entre 4 a 6 anos. As amostras de FGC foram coletadas em 4 pontos do sulco gengival dos 12 dentes traumatizados e de 8 primeiros molares decíduos, os quais foram divididos em 5 grupos: molar (primeiro molar decíduo), sem alteração, obliteração do canal pulpar (OCP), reparo relacionado à reabsorção (RRR) e necrose pulpar (NP). As proteínas do FCG foram submetidas espectrometria de massa em tandem de ionização por eletrovaporização, para identificação e caracterização. Oito crianças com 5 anos de idade, em média. 436 proteínas/peptídeos únicos foram encontrados neste estudo. 43 (9,86%) estavam no grupo Sem alteração, 92 (21,10%) no grupo OCP, 23 (5,28%) no grupo RRR, 16 (3,67%) no grupo NP, 114 (26,15%) no grupo molar. Todos os grupos revelaram as seguintes funções peptídeos / proteínas: resposta imune / degradação celular e reciclagem / reparo e manutenção / processo enzimático / ligação celular / sinalização celular / diferenciação celular / migração celular / componentes estruturais / atividade antioxidante. Funções proteicas relacionadas aos grupos: grupo molar desempenhou papel no processo de homeostase. As proteínas do grupo sem alteração: I6L9F6_HUMAN, NEB2_HUMAN, Q5T0H8_HUMAN, H0YJG4_HUMAN estão relacionadas ao tecido nervoso; e, TET1_HUMAN à diferenciação odontoblástica. As proteínas do grupo RRR: CALX_HUMAN, B8ZZF0_HUMAN estão relacionadas à senescência; e a mutação de KMT2D_HUMAN está associada à deformação esquelética. As proteínas do grupo PCO: CATA_HUMAN está associada à resposta de hipóxia, transformação de fibroblastos e diferenciação de osteoblastos; MTA70_HUMAN diferenciação de células-tronco; ITPR2_HUMAN libera íon de cálcio no citosol. As proteínas do grupo da fístula: Q8TAS6_HUMAN está relacionada ao desenvolvimento do tecido neuronal; E9PDR3_HUMAN à liberação de neurotransmissores, divisão e morte celular; B4DT36_HUMAN desempenha um papel na condução do axônio; C9JN07_HUMAN

relaciona-se ao processo mitótico; RSF1_HUMAN ao reparo de DNA; Q19KS2_HUMAN à defesa imunológica. Concluindo, o perfil dos dentes decíduos que sofreram trauma e tiveram diferentes tipos de sequelas foi caracterizado por diferentes proteínas. O grupo molar exibiu homeostase. Grupo sem alteração, as proteínas desempenharam um papel na manutenção do tecido nervoso. As proteínas do grupo PCO estavam envolvidas na transformação e diferenciação celular para atingir a obliteração do canal radicular. As proteínas do grupo RRR revelaram um processo de senescência. No grupo de fístula, as proteínas parecem desempenhar um papel para cercar o local da inflamação.

Palavras-chave: Proteoma. Líquido do Sulco Gengival. Traumatismos Dentários. Dente decíduo.

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LIST OF ABBREVIATION AND ACRONYMS

TDI	Traumatic dental injuries
GCF	Gingival Crevicular Fluid
PN	Pulp Necrosis
PCO	Pulp Canal Obliteration
RRR	Repair-Related Resorption
ROS	Reactive Oxygen Species
MMP-9	Matrix metalloproteinase-9
DSP	Dentine Sialoprotein

SUMÁRIO

1 INTRODUCTION

1 INTRODUCTION

Traumatic dental injuries (TDI) often happens in early childhood because falls occurs when children is learning to walk due to undeveloped motor coordination (Odersjö et al. 2018). The most common incidence of TDI is between 1 and 3 years-old (Cardoso and de Carvalho Rocha 2002) and incisors are the most affected teeth (Cardoso and de Carvalho Rocha 2002; Oliveira et al. 2007). Besides the age, other factors influence on TDI occurrence as pacifier use, lack of lip seal, open bite, and overjet (Oliveira et al. 2007; Kramer et al. 2015; Feldens et al. 2016). Intrusive luxation, avulsion, and crown root fracture are the most frequent TDI types (Kramer et al. 2016). Additionally, children with concussion, subluxation, and lateral luxation seek treatment in currently daily routine of Pediatric Dentistry clinics. TDI sequelae in deciduous teeth results in tooth discoloration, enamel/dentin/pulp fracture, pulp calcification/obliteration, and necrosis; the possible treatment can be follow-up, filling, pulpotomy, pulpectomy, and extraction (Robertson et al. 1997; Cardoso and Rocha 2004; Holan 2004; Qassem et al. 2014).

TDI monitoring is important because signs and symptoms of the sequelae can appear either right after the trauma (one or two months) or 1-2 years later (Qassem et al. 2015; Lauridsen et al. 2017b, 2017a). Because the intrinsic correlation between the root of primary teeth and the bud of permanent teeth, the following-up is important to prevent future damage to permanent successor tooth (Lauridsen et al. 2017c) (Malmgren et al. 2016). Consequently, TDI major sequelae in permanent bud teeth can be crown dilaceration; odontoma-like; partial or complete arrest of root; enamel hypoplasia; and root dilacerations (Kramer et al. 2016). Thus, follow-up appointments are as important as the first appointment after injury. Moreover, children who had TDI in primary dentition are more likely to have another dental injury in permanent dentition (Goettems et al. 2017).

The clinical examination is the main method to diagnosis and monitoring TDI, and radiograph is the most used auxiliary method (Gröndahl and Gröndahl 1983; Rody et al. 2014). However, radiographs have disadvantages as: two-dimensional image of a three-dimensional structure and superimposition of unrelated anatomical structures (Lofthag-Hansen et al. 2007), for example the buds of permanent successor. To

overcome these obstacles, the use of adjuvant methodologies is interesting to propose diagnosis in early stages of TDI sequelae.

Currently, molecular biology has been used in both laboratory and clinics to aid in diagnosis due to its sensitivity and specificity. Proteomics is a good example of this remarkable methodology (Khurshid et al. 2017; Ghallab 2018; Mastrangelo et al. 2018; Toker et al. 2018). Proteomics is the study on how the proteins behave and responds during health and disease process (Khurshid et al. 2017), by using proteins/peptides as biomarkers. The literature reports the use of laboratorial procedures to find those biomarkers in tissue (Accorsi-Mendonça et al. 2013; Bhalla et al. 2014), periapical exudate (Rechenberg et al. 2014; Pattamapun et al. 2017), and gingival crevicular fluid (GCF) collection (Kumar et al. 2013; Silva-Boghossian et al. 2013; Rody et al. 2014).

Several proteomics studies are related to Dentistry, such as periodontal disease (Ghallab 2018; Mastrangelo et al. 2018) and endodontic pathological processes (Shin et al. 2011; Accorsi-Mendonça et al. 2013). A close relation between dental pulp and periodontium tissues exists, that is, the convergence of both diseases is the development of inflammation culminating in periodontal bone degradation (Wahlgren et al. 2002; Shin et al. 2011). Additionally, proteins from GCF have been used in studies on injured pulp, tooth resorption, periapical lesions and pain in endodontic treatment (Awawdeh et al. 2002; Shin et al. 2011; Dezerega et al. 2012; Kumar et al. 2013; Bhalla et al. 2014; Bıçakcı et al. 2016), and resorption of deciduous tooth (Mah and Prasad 2004; Kereshanan et al. 2008; Rody et al. 2014). Therefore, the peptides/proteins related the sequelae of TDI in primary tooth as pulp necrosis (PN), pulp canal obliteration (PCO), repair-related resorption (RRR) and no alteration, could help in the early diagnosis, prognosis, and treatment, to attenuate and reduce the sequelae on both the primary and permanent teeth.

2 OBJECTIVE

2 OBJECTIVE

This study aimed to characterize the proteins/peptides in GCF of primary tooth with different sequelae of TDI to clarify the proteins/peptides functions in order to contribute in the diagnosis of pulp and periodontal conditions.

3 MATERIAL AND METHODS

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Sample selection

The present study was approved by Institutional Review Board of Bauru School of Dentistry, University of São Paulo (protocol no. CAAE: 48100115.9.0000.5417) (Annex 1). All parents/legal guardians were instructed on the research and signed a free and clarified consent form and the assent form was made in ludic way for the children, in the presence of their parents/legal guardians. The study group consisted of children who had a TDI in the municipal schools. The inclusion criteria were: children aged from 4 to 6 years, both genders, with at least one traumatized primary tooth presenting discoloration, without crown fracture, and without distinction about the time of injury.

Study groups

The experimental group consisted of twelve GCF samples of TDI teeth. The molar group included GCF samples of 8 left maxillary primary first molar (#64) of the same children who had TDI. In total the study comprised 8 children.

GCF collection

The supragingival biofilm was removed with dental prophylaxis. Each tooth was dried for 5 seconds with compressed air and isolated from saliva with a cotton roll. The GCF samples were collected in 4 points of the gingival sulcus of both the traumatized tooth and the primary first molar (control) as described previously (Silva-Boghossian et al. 2013) with the aid of Periopaper strip (ProFlow Inc., Amityville, NY, USA). The collection was made inserting gently the strips into the selected subgingival sites and left there for 30s (Carneiro et al. 2012). After collection the strips were stored in Eppendorf tubes at -80°C for posterior analysis.

Sample preparation

The four strips of each tooth were stored in one Eppendorf tube. Before the elution, the orange part of the Periopaper was removed. Proteins were eluted from the strips with 200 µl of 50 mM NH4HCO3, pH 7.8, sonicated for 1 minute followed by centrifugation (Eppendorf, Parkway, NY, USA) at 14000xg for 15 minutes to collect the elution (Zimmerman et al. 2013). This was repeated three times to elute all proteins from the paper strips. The total protein concentration was assessed by Micro Bicinchoninic acid (MicroBCA^{TM}) Assay (Thermo Scientific, Rockford, IL, USA). A protein amount around 6µg was the minimum amount found in the samples, so the microBCA was made in just few samples for test.

After the elution all the remaining samples were dried in a rotary evaporator. Following, the samples were denatured and reduced by the addition of 50µL of solution 1 (4M urea, 10 mM dithiothreitol (DTT), 50mM NH4HCO3, pH 7.8), for 1 hour in room temperature (RT). Elapsed that time, dilution with 150µl of solution 2 (50mM NH4HCO3, pH 7.8), tryptic digestion was carried out for 18 h at 37°C in bath water, after the addition of 4% (w/w) sequencing-grade trypsin (Promega, Madison, WI, USA) (Zimmerman et al. 2013). Finally, the sample were dried again in a rotary evaporator, de-salted by C18 Pipette Tips (Millipore, USA), dried, and subjected to mass spectrometry analyses (Siqueira et al. 2007).

Mass Spectrometry (MS) Analysis

Peptide separation and mass spectrometric analyses were carried out with a nano-HPLC Proxeon (Thermo Scientific, San Jose, CA, USA) which allows in-line liquid chromatography with the 75µm x 10cm capillary column (Pico TipTM EMITTER, New Objective, Woburn, MA) filled with C18 resin of 5mm diameter and 200Å pores sizes (Michrom BioResources, Auburn, CA) linked to mass spectrometer (LTQ-Velos, Thermo Scientific, San Jose, CA, USA) using an electrospray ionization in a survey scan in the range of m/z values 390–2000 tandem MS/MS. The equivalent of about 6µg of each dried sample were re-suspended in 10µl of 0.1% formic acid and then subjected to reversed-phase LC-ESI-MS/MS. The nano-flow reversed-phase HPLC was developed with linear gradient of 85 minutes ranging from 0% to 100% of solvent

B (97.5% acetonitrile, 0.1% formic acid) at a flow rate of 200 nl/min with a maximum pressure of 280 bar. Electrospray voltage and the temperature of the ion transfer capillary were 1.8 kV and 250ºC respectively (Silva-Boghossian et al. 2013).

Database search and protein identification

All MS/MS spectra from LC-ESI-MS/MS were search against human protein database (UniPROT and TREMBL, Swiss Institute of Bioinformatics, Geneva, Switzerland, http://ca.expasy.org) using SEQUEST and Proteome Discoverer 1.3 software (Thermo, USA), using at least two peptides. The SEQUEST filter criteria applied to MS/MS spectra were: 1.5; 2,5; 3,1; 3.1; 4.5 for the XCorr applied in addition to the Percolator filter. Search results were filtered at a false discovery rate of 1% using a reverse database search strategy (Siqueira et al. 2012). After identification of the proteomic profile, some proteins had their biological functions verified through the access number using the database www.uniprot.org.

4 RESULTS

4 RESULTS

Eight children aged 5 years-old in average met the inclusion criteria. All TDI occurred in maxillary primary incisors totalizing 12 teeth (Table 1). The molar group comprised 8 teeth. Data description about GCF collection is on Table 1.

Table 1. Sample distribution regarding age, TDI type, tooth color, GCF collection, and time of trauma. (Number of children = 8).

Name	Age (years)	Traumatized tooth -GCF collection	Tooth Color	Time of the trauma	Molar group - GCF collection
AJMR	4	61; 51	61 – darkish; 51 - normal	not aware	64
APN	5	61	61 - yellowish	not aware	64
DHOP	6	51F*; 61	51 – greyish; 61 yellowish	not aware	64
ERM	5	61	61- greyish	1 month ago	64
KIS	6	61	61- darkish	Five years ago	64
LPJ	5	61	61 - yellowish	not aware	64
MVTM	5	51; 61	51 – greyish; 61 normal	Three and half years ago	64
WLJ	5	51;61	61 – alteration; 51 normal	not aware	64
Mean	5	-			-

*51F – presence of fistulae

Radiographic data regarding injured teeth is described in Table 2. The TDI radiograph is in the Appendix I.

Table 2. Radiographic description of TDI, and their adjacent teeth (number of children = 8; number of traumatized teeth = 12)

Patient	Date	Tooth	Radiograph signals	Probable pulp diagnosis
AJMR	21/10/2015	52*	no change	Vital
		51•	obliteration	Vital
		61•	RRR	Vital
		62*	change	Vital
APN	26/11/2015	51*	no change	Vital
		61•	obliteration	Vital
		62*	no change	Vital
DHOP	26/11/2015	52*	no change	Vital
		51•	periapical inflammation	Necrotic
		61•	obliteration	Vital
		62*	no change	Vital
ERM	22/10/2015	51*	no change	vital
		61•	no change	Vital
		62*	no change	Vital
KIS	20/10/2015	52*	no change	Vital
		51#	absent	-
		61•	RRR	Vital
		62*	no change	Vital
LPJ	02/03/2016	51*	no change	Vital
		61•	obliteration	Vital
		62*	no change	Vital
MVTM	20/10/2015	52*	no change	Vital
		51•	no change	Vital
		61•	no change	Vital
		62*	no change	Vital
WLJ	25/11/2015	52*	no change	Vital
		51•	obliteration	Vital
		61•	obliteration	Vital
		62*	no change	Vital

• Traumatized tooth
* Tooth which was not injured
# missing tooth

After protein elution from the paper strip and trypsinization, equal amounts of peptides were subjected to nanoscale LC- ESI-MS/MS. One run per tooth were carried out. The base-peak chromatogram for reversed-phase chromatography monitored by the mass spectrometer represents the intensity of all peptide ions in the sample in a single scan. GCF proteome from all tooth showed a consistent elution of protein/peptides range from 20 to 40 min (Figure 1).

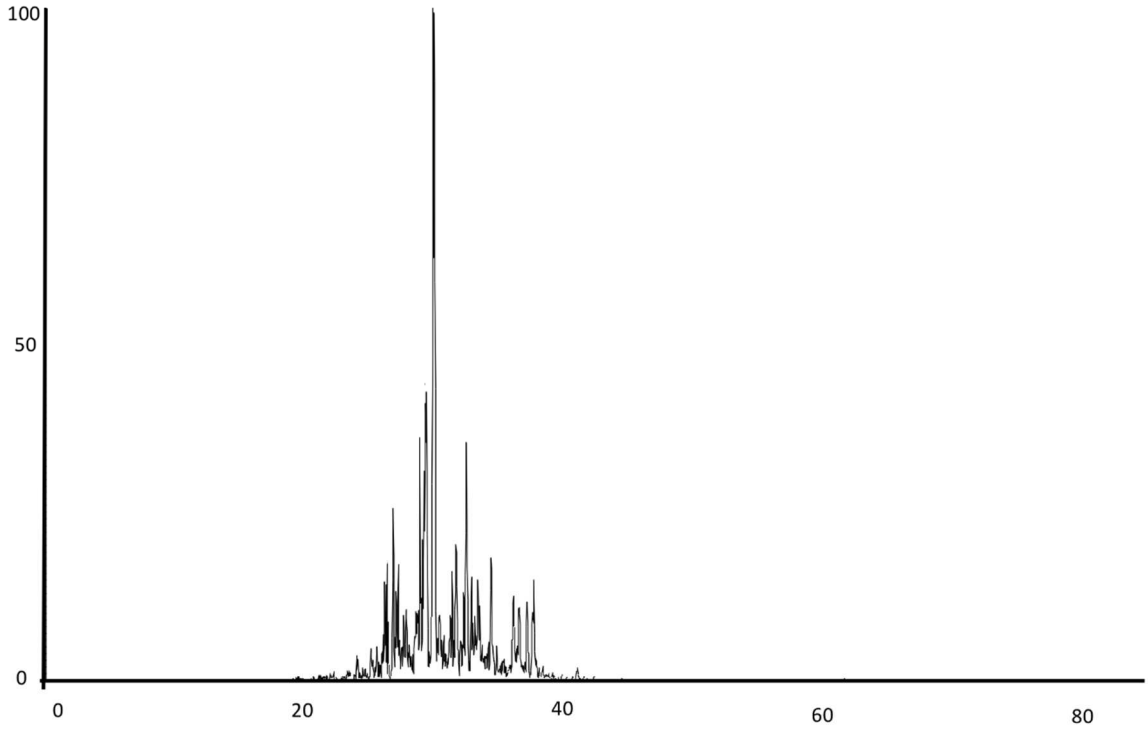

Figure 1: Example of base-peak chromatogram of a tooth.

The teeth were divided into the following groups based on the similar characteristics: Molar group all 8 left deciduous maxillary first molar; No alteration group – teeth: ERM 61, MVTM 51 and 61; PCO group – teeth: AJMR 51, APN 61, DHOP 61, LPJ 61, WLJ 51 and 61; RRR group – teeth: AJMR 61 and KIS 61; PN group – teeth DHOP 51.

The distribution of peptides/proteins among the groups is described in Venn Diagram (Bioinformatics & Evolutionary Genomics, BELGIUM) (Figure 2). Venn Diagram described all possible logical relation among the groups. Thus, 436 single proteins/peptides were found in this study (Table 3). Of all 436 proteins/peptides, 43 (9.86%) were in No alteration group, 92 (21.10%) in PCO group, 23 (5.28%) in RRR group, 16 (3.67%) in PN group, 114 (26.15%) in molar group.

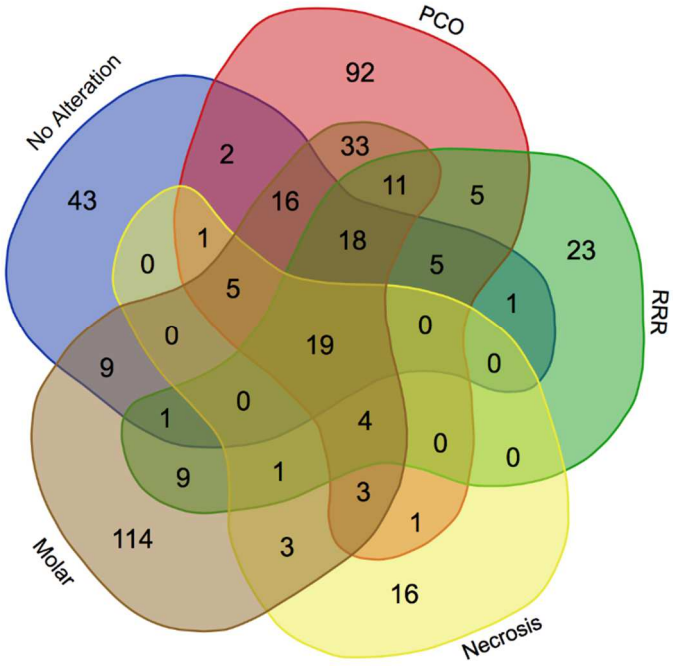

Figure 2 – Venn Diagram screening proteins found in the groups.

Table 3: Single proteins/peptides among groups

Groups	Entry name	Protein names
Molar x Necrosis x No Alteration x PCO x RRR	B4DL87_HUMAN	cDNA FLJ52243, highly similar to Heat-shock protein beta-1 OS=Homo sapiens PE=2 SV=1 -
	F6KPG5_HUMAN	Albumin (Fragment) OS=Homo sapiens PE=2 SV=1 -
	BASP1_HUMAN	Brain acid soluble protein 1 OS=Homo sapiens GN=BASP1 PE=1 SV=2 -
	B4E1T1_HUMAN	cDNA FLJ54081, highly similar to Keratin, type II cytoskeletal 5 OS=Homo sapiens PE=2 SV=1 -
	HPT_HUMAN	Haptoglobin OS=Homo sapiens GN=HP PE=1 SV=1 -
	B4DWU6_HUMAN	cDNA FLJ51361, highly similar to Keratin, type II cytoskeletal 6A OS=Homo sapiens PE=2 SV=1 -
	S10A8_HUMAN	Protein S100-A8 OS=Homo sapiens GN=S100A8 PE=1 SV=1 -
	Q71V99_HUMAN	Peptidyl-prolyl cis-trans isomerase OS=Homo sapiens PE=2 SV=1 -
	B8ZZQ6_HUMAN	Prothymosin alpha OS=Homo sapiens GN=PTMA PE=1 SV=1 -
	A2MG_HUMAN	Alpha-2-macroglobulin OS=Homo sapiens GN=A2M PE=1 SV=3 -
	IGKC_HUMAN	Ig kappa chain C region OS=Homo sapiens GN=IGKC PE=1 SV=1 -
	FIBA_HUMAN	Fibrinogen alpha chain OS=Homo sapiens GN=FGA PE=1 SV=2 -
	ENOA_HUMAN	Alpha-enolase OS=Homo sapiens GN=ENO1 PE=1 SV=2 -
	CALL3_HUMAN	Calmodulin-like protein 3 OS=Homo sapiens GN=CALML3 PE=1 SV=2 -
	B1AN48_HUMAN	Small proline-rich protein 3 (Fragment) OS=Homo sapiens GN=SPRR3 PE=1 SV=4 -
	S10A9_HUMAN	Protein S100-A9 OS=Homo sapiens GN=S100A9 PE=1 SV=1 -

	TYB4_HUMAN	Thymosin beta-4 OS=Homo sapiens GN=TMSB4X PE=1 SV=2 -
	B4E1B2_HUMAN	cDNA FLJ53691, highly similar to Serotransferrin OS=Homo sapiens PE=2 SV=1 -
	1433S_HUMAN	14-3-3 protein sigma OS=Homo sapiens GN=SFN PE=1 SV=1 -
Molar x No Alteration x PCO x RRR	PROF1_HUMAN	Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2 -
	Q53HE2_HUMAN	Triosephosphate isomerase (Fragment) OS=Homo sapiens PE=2 SV=1 -
	H3BQ34_HUMAN	Pyruvate kinase OS=Homo sapiens GN=PKM PE=1 SV=1 -
	PLSL_HUMAN	Plastin-2 OS=Homo sapiens GN=LCP1 PE=1 SV=6 -
	GSTP1_HUMAN	Glutathione S-transferase P OS=Homo sapiens GN=GSTP1 PE=1 SV=2 -
	MYH9_HUMAN	Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4 -
	B4E1H9_HUMAN	Phosphoglycerate kinase OS=Homo sapiens PE=2 SV=1 -
	TYB10_HUMAN	Thymosin beta-10 OS=Homo sapiens GN=TMSB10 PE=1 SV=2 -
	E7EQB2_HUMAN	Lactotransferrin (Fragment) OS=Homo sapiens GN=LTF PE=1 SV=1 -
	K1C14_HUMAN	Keratin, type I cytoskeletal 14 OS=Homo sapiens GN=KRT14 PE=1 SV=4 -
	Q8WVW5_HUMAN	Putative uncharacterized protein (Fragment) OS=Homo sapiens PE=2 SV=1 -
	K1C10_HUMAN	Keratin, type I cytoskeletal 10 OS=Homo sapiens GN=KRT10 PE=1 SV=6 -
	SMR3B_HUMAN	Submaxillary gland androgen-regulated protein 3B OS=Homo sapiens GN=SMR3B PE=1 SV=2 -
	Q4VY20_HUMAN	14-3-3 protein beta/alpha (Fragment) OS=Homo sapiens GN=YWHAB PE=1 SV=1 -
	IGHG1_HUMAN	Ig gamma-1 chain C region OS=Homo sapiens GN=IGHG1 PE=1 SV=1 -
	THIO_HUMAN	Thioredoxin OS=Homo sapiens GN=TXN PE=1 SV=3 -
	NGAL_HUMAN	Neutrophil gelatinase-associated lipocalin OS=Homo sapiens GN=LCN2 PE=1 SV=2 -
	B7Z6P1_HUMAN	cDNA FLJ53662, highly similar to Actin, alpha skeletal muscle OS=Homo sapiens PE=2 SV=1 -
Molar x Necrosis x No Alteration x PCO	CO3_HUMAN	Complement C3 OS=Homo sapiens GN=C3 PE=1 SV=2 -
	A0A024R6I7_HUMAN	Serpin peptidase inhibitor, clade A (Alpha-1 antiproteinase, antitrypsin), member 1, isoform CRA_a OS=Homo sapiens GN=SERPINA1 PE=3 SV=1 -
	A6XMH1_HUMAN	Transthyretin OS=Homo sapiens PE=2 SV=1 -
	CYTB_HUMAN	Cystatin-B OS=Homo sapiens GN=CSTB PE=1 SV=2 -
	A0A024R528_HUMAN	Interleukin 1 receptor antagonist, isoform CRA_a OS=Homo sapiens GN=IL1RN PE=3 SV=1 -
Molar x Necrosis x PCO x RRR	B3KPZ8_HUMAN	cDNA FLJ32530 fis, clone SMINT2000185, highly similar to TRANSKETOLASE (EC 2.2.1.1) OS=Homo sapiens PE=2 SV=1 -
	GDIR2_HUMAN	Rho GDP-dissociation inhibitor 2 OS=Homo sapiens GN=ARHGDIB PE=1 SV=3 -
	A1A4E9_HUMAN	Keratin 13 OS=Homo sapiens GN=KRT13 PE=1 SV=1 -
	ANXA1_HUMAN	Annexin A1 OS=Homo sapiens GN=ANXA1 PE=1 SV=2 -
No Alteration x PCO x RRR	Q5T3N1_HUMAN	Annexin (Fragment) OS=Homo sapiens GN=ANXA1 PE=1 SV=1 -
	Q5U071_HUMAN	High-mobility group box 2 OS=Homo sapiens PE=2 SV=1 -
	VIME_HUMAN	Vimentin OS=Homo sapiens GN=VIM PE=1 SV=4 -

	B7Z747_HUMAN	cDNA FLJ51120, highly similar to Matrix metalloproteinase-9 (EC 3.4.24.35) OS=Homo sapiens PE=2 SV=1 -
	Q9BRL5_HUMAN	CALM3 protein OS=Homo sapiens PE=1 SV=1 -
Necrosis x No Alteration x PCO	A0A075B6K9_HUMAN	Ig lambda-2 chain C regions (Fragment) OS=Homo sapiens GN=IGLC2 PE=4 SV=1 -
Molar x No Alteration x PCO	F8W696_HUMAN	Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1 -
	G3P_HUMAN	Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3 -
	A8K5I6_HUMAN	cDNA FLJ78643, highly similar to Homo sapiens cornulin (CRNN), mRNA OS=Homo sapiens PE=2 SV=1 -
	C0JYZ2_HUMAN	Titin OS=Homo sapiens GN=TTN PE=4 SV=1 -
	E7ERU0_HUMAN	Dystonin OS=Homo sapiens GN=DST PE=1 SV=1 -
	Q6NSB3_HUMAN	Alpha-amylase (Fragment) OS=Homo sapiens GN=AMY1A PE=2 SV=1 -
	D6RFG5_HUMAN	Annexin (Fragment) OS=Homo sapiens GN=ANXA3 PE=1 SV=1 -
	K7EJ44_HUMAN	Profilin 1, isoform CRA_b OS=Homo sapiens GN=PFN1 PE=1 SV=1 -
	H0YGX7_HUMAN	Rho GDP-dissociation inhibitor 2 (Fragment) OS=Homo sapiens GN=ARHGDIB PE=1 SV=1 -
	B5BU38_HUMAN	Annexin OS=Homo sapiens GN=ANXA1 PE=2 SV=1 -
	H6VRF8_HUMAN	Keratin 1 OS=Homo sapiens GN=KRT1 PE=3 SV=1 -
	V9GYE3_HUMAN	Apolipoprotein A-II OS=Homo sapiens GN=APOA2 PE=1 SV=1 -
	B2R4M6_HUMAN	Protein S100 OS=Homo sapiens PE=2 SV=1 -
	A1BG_HUMAN	Alpha-1B-glycoprotein OS=Homo sapiens GN=A1BG PE=1 SV=4 -
	Q5T123_HUMAN	SH3 domain-binding glutamic acid-rich-like protein 3 OS=Homo sapiens GN=SH3BGRL3 PE=1 SV=1 -
	K1C9_HUMAN	Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3 -
Molar x No Alteration x RRR	H12_HUMAN	Histone H1.2 OS=Homo sapiens GN=HIST1H1C PE=1 SV=2 -
Molar x PCO x RRR	FABP5_HUMAN	Fatty acid-binding protein, epidermal OS=Homo sapiens GN=FABP5 PE=1 SV=3 -
	A1L407_HUMAN	Histone cluster 1, H1t OS=Homo sapiens GN=HIST1H1T PE=2 SV=1 -
	A8K9J7_HUMAN	Histone H2B OS=Homo sapiens PE=2 SV=1 -
	COR1A_HUMAN	Coronin-1A OS=Homo sapiens GN=CORO1A PE=1 SV=4 -
	H6VRG2_HUMAN	Keratin 1 OS=Homo sapiens GN=KRT1 PE=3 SV=1 -
	APOA1_HUMAN	Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1 -
	PERM_HUMAN	Myeloperoxidase OS=Homo sapiens GN=MPO PE=1 SV=1 -
	A0A0A0MS07_HUMAN	Ig gamma-1 chain C region (Fragment) OS=Homo sapiens GN=IGHG1 PE=1 SV=1 -
	B4DW52_HUMAN	cDNA FLJ55253, highly similar to Actin, cytoplasmic 1 OS=Homo sapiens PE=2 SV=1 -
	B4DNG6_HUMAN	Annexin OS=Homo sapiens PE=2 SV=1 -
	B4DI39_HUMAN	cDNA FLJ54328, highly similar to Heat shock 70 kDa protein 1 OS=Homo sapiens PE=2 SV=1 -
Molar x Necrosis x PCO	GRP78_HUMAN	78 kDa glucose-regulated protein OS=Homo sapiens GN=HSPA5 PE=1 SV=2 -
	B0I1S0_HUMAN	DYNC2H1 variant protein OS=Homo sapiens PE=2 SV=1 -

	H4_HUMAN	Histone H4 OS=Homo sapiens GN=HIST1H4A PE=1 SV=2 -
Molar x Necrosis x RRR	E7EUT5_HUMAN	Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=1 -
No Alteration x PCO	K1210_HUMAN	Uncharacterized protein KIAA1210 OS=Homo sapiens GN=KIAA1210 PE=2 SV=3 -
	ACTN1_HUMAN	Alpha-actinin-1 OS=Homo sapiens GN=ACTN1 PE=1 SV=2 -
No Alteration x RRR	F8W9J4_HUMAN	Dystonin OS=Homo sapiens GN=DST PE=1 SV=1 -
Molar x No Alteration	Q5T0H9_HUMAN	Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1 -
	B3KSI4_HUMAN	Transketolase OS=Homo sapiens PE=2 SV=1 -
	C9JKR2_HUMAN	Albumin, isoform CRA_k OS=Homo sapiens GN=ALB PE=1 SV=1 -
	F5H2R5_HUMAN	Rho GDP-dissociation inhibitor 2 (Fragment) OS=Homo sapiens GN=ARHGDIB PE=1 SV=1 -
	B3KRK8_HUMAN	cDNA FLJ34494 fis, clone HLUNG2005030, highly similar to VIMENTIN OS=Homo sapiens PE=2 SV=1 -
	INVO_HUMAN	Involucrin OS=Homo sapiens GN=IVL PE=1 SV=2 -
	G3V5X4_HUMAN	Nesprin-2 OS=Homo sapiens GN=SYNE2 PE=1 SV=1 -
	K22E_HUMAN	Keratin, type II cytoskeletal 2 epidermal OS=Homo sapiens GN=KRT2 PE=1 SV=2 -
	H15_HUMAN	Histone H1.5 OS=Homo sapiens GN=HIST1H1B PE=1 SV=3 -
PCO x RRR	ANXA3_HUMAN	Annexin A3 OS=Homo sapiens GN=ANXA3 PE=1 SV=3 -
	B4E216_HUMAN	cDNA FLJ57339, highly similar to Complement C3 OS=Homo sapiens PE=2 SV=1 -
	SRRM2_HUMAN	Serine/arginine repetitive matrix protein 2 OS=Homo sapiens GN=SRRM2 PE=1 SV=2 -
	B4DWQ3_HUMAN	Phosphoglycerate kinase OS=Homo sapiens PE=2 SV=1 -
	B7Z2X4_HUMAN	cDNA FLJ53327, highly similar to Gelsolin OS=Homo sapiens PE=2 SV=1 -
Necrosis x PCO	B4DUI5_HUMAN	Triosephosphate isomerase OS=Homo sapiens PE=2 SV=1 -
Molar x PCO	SBSN_HUMAN	Suprabasin OS=Homo sapiens GN=SBSN PE=1 SV=2 -
	H2A1H_HUMAN	Histone H2A type 1-H OS=Homo sapiens GN=HIST1H2AH PE=1 SV=3 -
	B5BU24_HUMAN	14-3-3 protein beta/alpha OS=Homo sapiens GN=YWHAB PE=2 SV=1 -
	HEMO_HUMAN	Hemopexin OS=Homo sapiens GN=HPX PE=1 SV=2 -
	D3DP16_HUMAN	Fibrinogen gamma chain, isoform CRA_a OS=Homo sapiens GN=FGG PE=4 SV=1 -
	Q5T985_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H2 OS=Homo sapiens GN=ITIH2 PE=1 SV=1 -
	TALDO_HUMAN	Transaldolase OS=Homo sapiens GN=TALDO1 PE=1 SV=2 -
	B7Z539_HUMAN	cDNA FLJ56954, highly similar to Inter-alpha-trypsin inhibitor heavy chain H1 OS=Homo sapiens PE=2 SV=1 -
	Q6PJF2_HUMAN	IGK@ protein OS=Homo sapiens GN=IGK@ PE=1 SV=1 -
	B4E380_HUMAN	Histone H3 OS=Homo sapiens PE=2 SV=1 -
	IGHG4_HUMAN	Ig gamma-4 chain C region OS=Homo sapiens GN=IGHG4 PE=1 SV=1 -
	ANT3_HUMAN	Antithrombin-III OS=Homo sapiens GN=SERPINC1 PE=1 SV=1 -
	LDHA_HUMAN	L-lactate dehydrogenase A chain OS=Homo sapiens GN=LDHA PE=1 SV=2 -
	PIP_HUMAN	Prolactin-inducible protein OS=Homo sapiens GN=PIP PE=1 SV=1 -
	B4E3A8_HUMAN	cDNA FLJ53963, highly similar to Leukocyte elastase inhibitor OS=Homo sapiens PE=2 SV=1 -

	B5ANL9_HUMAN	Beta globin chain (Fragment) OS=Homo sapiens GN=HBB PE=3 SV=1 -
	B4E022_HUMAN	cDNA FLJ56274, highly similar to Transketolase (EC 2.2.1.1) OS=Homo sapiens PE=2 SV=1 -
	H0YA55_HUMAN	Serum albumin (Fragment) OS=Homo sapiens GN=ALB PE=1 SV=1 -
	B4DE36_HUMAN	Glucose-6-phosphate isomerase OS=Homo sapiens PE=2 SV=1 -
	K22O_HUMAN	Keratin, type II cytoskeletal 2 oral OS=Homo sapiens GN=KRT76 PE=1 SV=2 -
	B7ZAL5_HUMAN	cDNA, FLJ79229, highly similar to Lactotransferrin (EC 3.4.21.-) OS=Homo sapiens PE=2 SV=1 -
	B4DRR0_HUMAN	cDNA FLJ53910, highly similar to Keratin, type II cytoskeletal 6A OS=Homo sapiens PE=2 SV=1 -
	SH3L1_HUMAN	SH3 domain-binding glutamic acid-rich-like protein OS=Homo sapiens GN=SH3BGRL PE=1 SV=1 -
	B4DRW1_HUMAN	cDNA FLJ55805, highly similar to Keratin, type II cytoskeletal 4 OS=Homo sapiens PE=2 SV=1 -
	HSPB1_HUMAN	Heat shock protein beta-1 OS=Homo sapiens GN=HSPB1 PE=1 SV=2 -
	B7Z5Q2_HUMAN	cDNA FLJ58075, highly similar to Ceruloplasmin (EC 1.16.3.1) OS=Homo sapiens PE=2 SV=1 -
	H7C5H1_HUMAN	Complement factor B (Fragment) OS=Homo sapiens GN=CFB PE=1 SV=1 -
	Q5ZEY3_HUMAN	Glyceraldehyde-3-phosphate dehydrogenase (Fragment) OS=Homo sapiens GN=GAPD PE=2 SV=1 -
	RIF1_HUMAN	Telomere-associated protein RIF1 OS=Homo sapiens GN=RIF1 PE=1 SV=2 -
	MOES_HUMAN	Moesin OS=Homo sapiens GN=MSN PE=1 SV=3 -
	B7Z4U6_HUMAN	cDNA FLJ55803, highly similar to Gelsolin OS=Homo sapiens PE=2 SV=1 -
	ACTN4_HUMAN	Alpha-actinin-4 OS=Homo sapiens GN=ACTN4 PE=1 SV=2 -
	ACTA_HUMAN	Actin, aortic smooth muscle OS=Homo sapiens GN=ACTA2 PE=1 SV=1 -
Molar x RRR	K7EQ48_HUMAN	Glucose-6-phosphate isomerase OS=Homo sapiens GN=GPI PE=1 SV=2 -
	M3K6_HUMAN	Mitogen-activated protein kinase kinase kinase 6 OS=Homo sapiens GN=MAP3K6 PE=1 SV=3 -
	H3BQN4_HUMAN	Fructose-bisphosphate aldolase OS=Homo sapiens GN=ALDOA PE=1 SV=1 -
	F8VU57_HUMAN	Probable E3 ubiquitin-protein ligase HECTD4 (Fragment) OS=Homo sapiens GN=HECTD4 PE=4 SV=1 -
	A0A087WWY3_HUMAN	Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=1 -
	K1C19_HUMAN	Keratin, type I cytoskeletal 19 OS=Homo sapiens GN=KRT19 PE=1 SV=4 -
	D6RCA8_HUMAN	Annexin (Fragment) OS=Homo sapiens GN=ANXA3 PE=1 SV=1 -
	D6R904_HUMAN	Tropomyosin alpha-3 chain OS=Homo sapiens GN=TPM3 PE=1 SV=1 -
	B4DHR1_HUMAN	cDNA FLJ53009, highly similar to Calreticulin OS=Homo sapiens PE=2 SV=1 -
Molar x Necrosis	D6RF35_HUMAN	Vitamin D-binding protein OS=Homo sapiens GN=GC PE=1 SV=1 -
	B3KTV0_HUMAN	cDNA FLJ38781 fis, clone LIVER2000216, highly similar to HEAT SHOCK COGNATE 71 kDa PROTEIN OS=Homo sapiens PE=2 SV=1 -
	B4DNL5_HUMAN	Protein disulfide-isomerase OS=Homo sapiens PE=2 SV=1 -
No Alteration	H3BRY3_HUMAN	Coronin OS=Homo sapiens GN=CORO1A PE=1 SV=1 -
	B4DXL2_HUMAN	cDNA FLJ58638, highly similar to Homo sapiens Rho GTPase activating protein 28 (ARHGAP28), transcript variant 1, mRNA OS=Homo sapiens PE=2 SV=1 -
	B4E1W5_HUMAN	cDNA FLJ58877, highly similar to FXYD domain-containing ion transport regulator 5 OS=Homo sapiens PE=2 SV=1 -
	Q5T0H8_HUMAN	Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1 -
	RAG1_HUMAN	V(D)J recombination-activating protein 1 OS=Homo sapiens GN=RAG1 PE=1 SV=2 -
	I6L9F6_HUMAN	NEFL protein OS=Homo sapiens GN=NEFL PE=1 SV=1 -

Q5JQ13_HUMAN	Vinculin (Fragment) OS=Homo sapiens GN=VCL PE=1 SV=1 -
B7Z4I6_HUMAN	cDNA FLJ55581, highly similar to AF4/FMR2 family member 3 (Fragment) OS=Homo sapiens PE=2 SV=1 -
DAAM2_HUMAN	Disheveled-associated activator of morphogenesis 2 OS=Homo sapiens GN=DAAM2 PE=1 SV=3 -
PP4R4_HUMAN	Serine/threonine-protein phosphatase 4 regulatory subunit 4 OS=Homo sapiens GN=PPP4R4 PE=1 SV=1 -
E9PB13_HUMAN	Kinase suppressor of Ras 2 OS=Homo sapiens GN=KSR2 PE=4 SV=1 -
Q6P1L4_HUMAN	PYGL protein (Fragment) OS=Homo sapiens GN=PYGL PE=2 SV=1 -
I3L1U9_HUMAN	Actin, cytoplasmic 2 (Fragment) OS=Homo sapiens GN=ACTG1 PE=1 SV=1 -
ATG2B_HUMAN	Autophagy-related protein 2 homolog B OS=Homo sapiens GN=ATG2B PE=1 SV=5 -
GLCI1_HUMAN	Glucocorticoid-induced transcript 1 protein OS=Homo sapiens GN=GLCCI1 PE=1 SV=1 -
GP158_HUMAN	Probable G-protein coupled receptor 158 OS=Homo sapiens GN=GPR158 PE=1 SV=1 -
A0A024QYV8_HUMAN	CP110 protein, isoform CRA_a OS=Homo sapiens GN=CP110 PE=4 SV=1 -
B7ZW05_HUMAN	AKAP13 protein (Fragment) OS=Homo sapiens GN=AKAP13 PE=2 SV=1 -
J3KRE2_HUMAN	Rho GDP-dissociation inhibitor 1 OS=Homo sapiens GN=ARHGDIA PE=1 SV=1 -
F2Z393_HUMAN	Transaldolase OS=Homo sapiens GN=TALDO1 PE=1 SV=1 -
H0YNA1_HUMAN	Protein FAM98B (Fragment) OS=Homo sapiens GN=FAM98B PE=1 SV=1 -
H0YJG4_HUMAN	Chromodomain-helicase-DNA-binding protein 8 (Fragment) OS=Homo sapiens GN=CHD8 PE=1 SV=1 -
FSIP2_HUMAN	Fibrous sheath-interacting protein 2 OS=Homo sapiens GN=FSIP2 PE=2 SV=4 -
PTN12_HUMAN	Tyrosine-protein phosphatase non-receptor type 12 OS=Homo sapiens GN=PTPN12 PE=1 SV=3 -
GPTC8_HUMAN	G patch domain-containing protein 8 OS=Homo sapiens GN=GPATCH8 PE=1 SV=2 -
F8WA11_HUMAN	CLIP-associating protein 1 OS=Homo sapiens GN=CLASP1 PE=1 SV=2 -
T1S9D5_HUMAN	MUC5AC (Fragment) OS=Homo sapiens GN=MUC5AC PE=4 SV=1 -
A0AUL6_HUMAN	ACTB protein (Fragment) OS=Homo sapiens GN=ACTB PE=2 SV=1 -
G3XAK3_HUMAN	CAP-Gly domain-containing linker protein 4 OS=Homo sapiens GN=CLIP4 PE=1 SV=1 -
Q8NEY2_HUMAN	Hepatocellular carcinoma-associated antigen OS=Homo sapiens GN=HCA107 PE=2 SV=1 -
FAK2_HUMAN	Protein-tyrosine kinase 2-beta OS=Homo sapiens GN=PTK2B PE=1 SV=2 -
G3V380_HUMAN	Alpha-actinin-1 (Fragment) OS=Homo sapiens GN=ACTN1 PE=1 SV=1 -
TET1_HUMAN	Methylcytosine dioxygenase TET1 OS=Homo sapiens GN=TET1 PE=1 SV=2 -
B4DHZ6_HUMAN	Transferrin, isoform CRA_c OS=Homo sapiens GN=TF PE=2 SV=1 -
PPR29_HUMAN	Protein phosphatase 1 regulatory subunit 29 OS=Homo sapiens GN=ELFN2 PE=1 SV=1 -
CAP1_HUMAN	Adenylyl cyclase-associated protein 1 OS=Homo sapiens GN=CAP1 PE=1 SV=5 -
B4DXY3_HUMAN	cDNA FLJ56517, highly similar to Heat shock 70 kDa protein 1L OS=Homo sapiens PE=2 SV=1 -
J3KPF0_HUMAN	Probable E3 ubiquitin-protein ligase HECTD4 OS=Homo sapiens GN=HECTD4 PE=1 SV=2 -

	B4DEF7_HUMAN	cDNA FLJ60062, highly similar to 78 kDa glucose-regulated protein OS=Homo sapiens PE=2 SV=1 -
	A8K7T1_HUMAN	cDNA FLJ76055, highly similar to Homo sapiens purinergic receptor P2Y, G-protein coupled, 12 (P2RY12), transcript variant 1, mRNA OS=Homo sapiens PE=2 SV=1 -
	NEB2_HUMAN	Neurabin-2 OS=Homo sapiens GN=PPP1R9B PE=1 SV=2 -
	Q86XU5_HUMAN	MYH9 protein (Fragment) OS=Homo sapiens GN=MYH9 PE=2 SV=1 -
	C9JPJ8_HUMAN	Palmitoyltransferase ZDHHC23 (Fragment) OS=Homo sapiens GN=ZDHHC23 PE=4 SV=1 -
PCO	HS90A_HUMAN	Heat shock protein HSP 90-alpha OS=Homo sapiens GN=HSP90AA1 PE=1 SV=5 -
	Q96IS6_HUMAN	HSPA8 protein (Fragment) OS=Homo sapiens GN=HSPA8 PE=1 SV=2 -
	B4E2Y9_HUMAN	cDNA FLJ58668, highly similar to Calreticulin OS=Homo sapiens PE=2 SV=1 -
	MTA70_HUMAN	N6-adenosine-methyltransferase 70 kDa subunit OS=Homo sapiens GN=METTL3 PE=1 SV=2 -
	B7Z5V2_HUMAN	cDNA FLJ54141, highly similar to Ezrin OS=Homo sapiens PE=2 SV=1 -
	TEX35_HUMAN	Testis-expressed sequence 35 protein OS=Homo sapiens GN=Tex35 PE=2 SV=1 -
	C9JFF0_HUMAN	Kinesin-like protein OS=Homo sapiens GN=KIF26A PE=1 SV=1 -
	I3L182_HUMAN	Serine/arginine repetitive matrix protein 2 (Fragment) OS=Homo sapiens GN=SRRM2 PE=1 SV=1 -
	A0A087WUE9_HUMAN	Symplekin OS=Homo sapiens GN=SYMPK PE=1 SV=1 -
	I3NI03_HUMAN	Protein disulfide-isomerase (Fragment) OS=Homo sapiens GN=P4HB PE=1 SV=1 -
	PA24B_HUMAN	Cytosolic phospholipase A2 beta OS=Homo sapiens GN=PLA2G4B PE=1 SV=2 -
	H7C070_HUMAN	Uncharacterized protein KIAA1109 (Fragment) OS=Homo sapiens GN=KIAA1109 PE=1 SV=1 -
	H13_HUMAN	Histone H1.3 OS=Homo sapiens GN=HIST1H1D PE=1 SV=2 -
	O60382_HUMAN	KIAA0324 (Fragment) OS=Homo sapiens GN=KIAA0324 PE=4 SV=1 -
	D6RF92_HUMAN	C-X-C motif chemokine OS=Homo sapiens GN=CXCL6 PE=3 SV=1 -
	ALKB5_HUMAN	RNA demethylase ALKBH5 OS=Homo sapiens GN=ALKBH5 PE=1 SV=2 -
	Q9UQC1_HUMAN	Heat shock protein 72 (Fragment) OS=Homo sapiens GN=HSP70-1 PE=3 SV=1 -
	E9PBD8_HUMAN	Lymphocyte-specific protein 1 (Fragment) OS=Homo sapiens GN=LSP1 PE=1 SV=1 -
	H2B1B_HUMAN	Histone H2B type 1-B OS=Homo sapiens GN=HIST1H2BB PE=1 SV=2 -
	A0A087X010_HUMAN	Ig gamma-1 chain C region OS=Homo sapiens GN=IGHG1 PE=1 SV=1 -
	ADGB_HUMAN	Androglobin OS=Homo sapiens GN=ADGB PE=2 SV=3 -
	B4DSX7_HUMAN	cDNA FLJ59047 OS=Homo sapiens PE=2 SV=1 -
	G3V544_HUMAN	Alpha-1-antitrypsin (Fragment) OS=Homo sapiens GN=SERPINA1 PE=1 SV=1 -
	LYSM2_HUMAN	LysM and putative peptidoglycan-binding domain-containing protein 2 OS=Homo sapiens GN=LYSMD2 PE=1 SV=1 -
	Q9BYF7_HUMAN	SCCA2b OS=Homo sapiens GN=SCCA2 PE=2 SV=1 -
	Q53HU8_HUMAN	Vimentin variant (Fragment) OS=Homo sapiens PE=2 SV=1 -
	Q13707_HUMAN	ACTA2 protein (Fragment) OS=Homo sapiens GN=ACTA2 PE=3 SV=1 -
	A0A087WWU8_HUMAN	Tropomyosin alpha-3 chain OS=Homo sapiens GN=TPM3 PE=1 SV=1 -
	Q53G71_HUMAN	Calreticulin variant (Fragment) OS=Homo sapiens PE=2 SV=1 -
	A0A0C4DFX2_HUMAN	Protein furry homolog OS=Homo sapiens GN=FRY PE=1 SV=1 -

A0A087WTR6_HUMAN	Protocadherin-15 OS=Homo sapiens GN=PCDH15 PE=4 SV=1 -
DYH5_HUMAN	Dynein heavy chain 5, axonemal OS=Homo sapiens GN=DNAH5 PE=1 SV=3 -
B3KPD3_HUMAN	cDNA FLJ31633 fis, clone NT2RI2003407, highly similar to Inner centromere protein (Fragment) OS=Homo sapiens PE=2 SV=1 -
A0A0B5HJK3_HUMAN	Truncated ALSM1 OS=Homo sapiens PE=4 SV=1 -
A0A087WTW5_HUMAN	CASP8-associated protein 2 OS=Homo sapiens GN=CASP8AP2 PE=1 SV=1 -
B4DUT7_HUMAN	cDNA FLJ57604, highly similar to GMP synthase (glutamine-hydrolyzing) (EC 6.3.5.2) OS=Homo sapiens PE=2 SV=1 -
Q5T085_HUMAN	Alpha-amylase (Fragment) OS=Homo sapiens GN=AMY1B PE=1 SV=1 -
H0YMT1_HUMAN	Talin-2 (Fragment) OS=Homo sapiens GN=TLN2 PE=1 SV=1 -
E1B2D1_HUMAN	Hemoglobin alpha-1 globin chain variant (Fragment) OS=Homo sapiens GN=HBA1 PE=3 SV=1 -
A8K6L7_HUMAN	cDNA FLJ78668, highly similar to Homo sapiens deleted in liver cancer 1 (DLC1), transcript variant 1, mRNA OS=Homo sapiens PE=2 SV=1 -
ITPR2_HUMAN	Inositol 1,4,5-trisphosphate receptor type 2 OS=Homo sapiens GN=ITPR2 PE=1 SV=2 -
E9PJP2_HUMAN	Protein SOGA3 OS=Homo sapiens GN=SOGA3 PE=1 SV=1 -
CENPF_HUMAN	Centromere protein F OS=Homo sapiens GN=CENPF PE=1 SV=2 -
B7Z1S3_HUMAN	cDNA FLJ56058, highly similar to Castor homolog 1 zinc finger protein OS=Homo sapiens PE=2 SV=1 -
B4DSK7_HUMAN	cDNA FLJ50196, highly similar to Peroxisome proliferator-activated receptor-binding protein (Fragment) OS=Homo sapiens PE=2 SV=1 -
C9JTX5_HUMAN	Actin, cytoplasmic 1 (Fragment) OS=Homo sapiens GN=ACTB PE=1 SV=1 -
KRR1_HUMAN	KRR1 small subunit processome component homolog OS=Homo sapiens GN=KRR1 PE=1 SV=4 -
ZN862_HUMAN	Zinc finger protein 862 OS=Homo sapiens GN=ZNF862 PE=2 SV=2 -
Q6ZTL7_HUMAN	cDNA FLJ44537 fis, clone UTERU3005049 OS=Homo sapiens PE=2 SV=1 -
B7Z9A0_HUMAN	cDNA FLJ56212, highly similar to Gelsolin OS=Homo sapiens PE=2 SV=1 -
B4E1L9_HUMAN	cDNA FLJ51603 OS=Homo sapiens PE=2 SV=1 -
HERC2_HUMAN	E3 ubiquitin-protein ligase HERC2 OS=Homo sapiens GN=HERC2 PE=1 SV=2 -
D3DPG0_HUMAN	Titin, isoform CRA_a OS=Homo sapiens GN=TTN PE=4 SV=1 -
TITIN_HUMAN	Titin OS=Homo sapiens GN=TTN PE=1 SV=4 -
C6KXN3_HUMAN	Lambda light chain of human immunoglobulin surface antigen-related protein (Fragment) OS=Homo sapiens GN=IgLC-rG PE=1 SV=1 -
V9HVZ7_HUMAN	Epididymis luminal protein 176 OS=Homo sapiens GN=HEL-176 PE=2 SV=1 -
FREM2_HUMAN	FRAS1-related extracellular matrix protein 2 OS=Homo sapiens GN=FREM2 PE=1 SV=2 -
F8VYN8_HUMAN	Centrosomal protein of 83 kDa OS=Homo sapiens GN=CEP83 PE=1 SV=1 -
B7Z2E6_HUMAN	14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1 -
Q6B823_HUMAN	Histone H4 (Fragment) OS=Homo sapiens PE=3 SV=1 -
B4DVG9_HUMAN	cDNA FLJ57007, highly similar to Microtubule-associated protein 9 OS=Homo sapiens PE=2 SV=1 -
U2AFL_HUMAN	U2 small nuclear ribonucleoprotein auxiliary factor 35 kDa subunit-related protein 1 OS=Homo sapiens GN=ZRSR1 PE=2 SV=2 -
B2RCA2_HUMAN	cDNA, FLJ95932, Homo sapiens polyamine modulated factor 1 binding protein 1(PMFBP1), mRNA OS=Homo sapiens PE=2 SV=1 -
UBR4_HUMAN	E3 ubiquitin-protein ligase UBR4 OS=Homo sapiens GN=UBR4 PE=1 SV=1 -
H7C0L5_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H4 (Fragment) OS=Homo sapiens GN=ITIH4 PE=1 SV=1 -

	A0A087WV66_HUMAN	Antigen KI-67 OS=Homo sapiens GN=MKI67 PE=1 SV=1 -
	LRR70_HUMAN	Leucine-rich repeat-containing protein 70 OS=Homo sapiens GN=LRRC70 PE=2 SV=1 -
	MYLK_HUMAN	Myosin light chain kinase, smooth muscle OS=Homo sapiens GN=MYLK PE=1 SV=4 -
	Q53FC7_HUMAN	Heat shock 70kDa protein 6 (HSP70B') variant (Fragment) OS=Homo sapiens PE=1 SV=1 -
	Q6PEJ8_HUMAN	HP protein OS=Homo sapiens GN=HP PE=2 SV=1 -
	MYH7B_HUMAN	Myosin-7B OS=Homo sapiens GN=MYH7B PE=1 SV=3 -
	YM012_HUMAN	Uncharacterized protein DKFZp434B061 OS=Homo sapiens PE=2 SV=2 -
	B5MC15_HUMAN	Cas-Br-M (Murine) ecotropic retroviral transforming sequence b, isoform CRA_a OS=Homo sapiens GN=CBLB PE=1 SV=1 -
	Q1HW68_HUMAN	ADAM21-like protein OS=Homo sapiens PE=2 SV=1 -
	MYCB2_HUMAN	E3 ubiquitin-protein ligase MYCBP2 OS=Homo sapiens GN=MYCBP2 PE=1 SV=3 -
	B4DMJ7_HUMAN	HCG2015269, isoform CRA_c OS=Homo sapiens GN=hCG_2015269 PE=2 SV=1 -
	Q59FC6_HUMAN	Tumor rejection antigen (Gp96) 1 variant (Fragment) OS=Homo sapiens PE=2 SV=1 -
	SYTL2_HUMAN	Synaptotagmin-like protein 2 OS=Homo sapiens GN=SYTL2 PE=1 SV=3 -
	S100P_HUMAN	Protein S100-P OS=Homo sapiens GN=S100P PE=1 SV=2 -
	A2BDK6_HUMAN	Microtubule-associated protein 1B OS=Homo sapiens GN=MAP1B PE=2 SV=1 -
	E7EVA0_HUMAN	Microtubule-associated protein OS=Homo sapiens GN=MAP4 PE=1 SV=1 -
	B7WPD9_HUMAN	Kinesin-like protein OS=Homo sapiens GN=KIF26B PE=3 SV=1 -
	ZN831_HUMAN	Zinc finger protein 831 OS=Homo sapiens GN=ZNF831 PE=2 SV=4 -
	ARRS_HUMAN	S-arrestin OS=Homo sapiens GN=SAG PE=1 SV=3 -
	M0QY24_HUMAN	Zinc finger protein 546 OS=Homo sapiens GN=ZNF546 PE=4 SV=1 -
	A8K4M9_HUMAN	cDNA FLJ78738, highly similar to Homo sapiens ankyrin repeat-containing cofactor-1 (ANCO1) mRNA (Fragment) OS=Homo sapiens PE=2 SV=1 -
	B4DVU1_HUMAN	cDNA FLJ53217, highly similar to Transketolase (EC 2.2.1.1) OS=Homo sapiens PE=2 SV=1 -
	Q53HF2_HUMAN	Heat shock 70kDa protein 8 isoform 2 variant (Fragment) OS=Homo sapiens PE=1 SV=1 -
	ALPK2_HUMAN	Alpha-protein kinase 2 OS=Homo sapiens GN=ALPK2 PE=2 SV=3 -
	A0A024RDD6_HUMAN	Uncharacterized protein OS=Homo sapiens GN=LOC285513 PE=4 SV=1 -
	CFA58_HUMAN	Cilia- and flagella-associated protein 58 OS=Homo sapiens GN=CFAP58 PE=1 SV=1 -
	CATA_HUMAN	Catalase OS=Homo sapiens GN=CAT PE=1 SV=3 -
RRR	A4D2J6_HUMAN	Phosphoglycerate mutase OS=Homo sapiens GN=PGAM2 PE=3 SV=1 -
	B4DJS0_HUMAN	cDNA FLJ56766, highly similar to Protein disulfide-isomerase (EC5.3.4.1) OS=Homo sapiens PE=2 SV=1 -
	KLH24_HUMAN	Kelch-like protein 24 OS=Homo sapiens GN=KLHL24 PE=2 SV=1 -
	I3L312_HUMAN	Protein disulfide-isomerase (Fragment) OS=Homo sapiens GN=P4HB PE=1 SV=2 -
	CCD96_HUMAN	Coiled-coil domain-containing protein 96 OS=Homo sapiens GN=CCDC96 PE=2 SV=2 -
	Q59GI3_HUMAN	I-kappa-B-related protein variant (Fragment) OS=Homo sapiens PE=2 SV=1 -
	H0Y5T1_HUMAN	CLIP-associating protein 1 (Fragment) OS=Homo sapiens GN=CLASP1 PE=1 SV=1 -

	LSP1_HUMAN	Lymphocyte-specific protein 1 OS=Homo sapiens GN=LSP1 PE=1 SV=1 -
	CALX_HUMAN	Calnexin OS=Homo sapiens GN=CANX PE=1 SV=2 -
	B8ZZF0_HUMAN	Protein phosphatase 1B (Fragment) OS=Homo sapiens GN=PPM1B PE=1 SV=2 -
	A1YBP1_HUMAN	Breast and ovarian cancer susceptibility protein 2 truncated variant OS=Homo sapiens GN=BRCA2 PE=2 SV=1 -
	F8VZU9_HUMAN	Myosin light polypeptide 6 OS=Homo sapiens GN=MYL6 PE=1 SV=1 -
	CC162_HUMAN	Coiled-coil domain-containing protein 162 OS=Homo sapiens GN=CCDC162P PE=2 SV=3 -
	Q2F831_HUMAN	Tyrosine 3-monooxygenasea/tryptophan 5-monooxygenase activation protein zeta (Fragment) OS=Homo sapiens PE=2 SV=1 -
	B0AZU6_HUMAN	cDNA, FLJ79536, highly similar to Heat shock 70 kDa protein 4 OS=Homo sapiens PE=2 SV=1 -
	Q7RTM4_HUMAN	Spectrin-like protein of the nuclear envelope and Golgi OS=Homo sapiens GN=SYNE1 PE=2 SV=1 -
	FBP12_HUMAN	Fatty acid-binding protein 12 OS=Homo sapiens GN=FABP12 PE=2 SV=2 -
	A0A087WWT3_HUMAN	Serum albumin OS=Homo sapiens GN=ALB PE=1 SV=1 -
	B4DWQ5_HUMAN	cDNA FLJ51655, highly similar to Actin-like protein 2 OS=Homo sapiens PE=2 SV=1 -
	K7EMV3_HUMAN	Histone H3 OS=Homo sapiens GN=H3F3B PE=1 SV=1 -
	H9A532_HUMAN	BCL6 corepressor-cyclin B3 fusion protein OS=Homo sapiens PE=2 SV=1 -
	KMT2D_HUMAN	Histone-lysine N-methyltransferase 2D OS=Homo sapiens GN=KMT2D PE=1 SV=2 -
	B7Z565_HUMAN	cDNA FLJ54739, highly similar to Alpha-actinin-1 OS=Homo sapiens PE=2 SV=1 -
Necrosis	C9JN07_HUMAN	HEPACAM family member 2 OS=Homo sapiens GN=HEPACAM2 PE=4 SV=1 -
	B4DT36_HUMAN	cDNA FLJ60876, highly similar to Semaphorin-6B OS=Homo sapiens PE=2 SV=1 -
	B7Z7S9_HUMAN	cDNA FLJ61724, highly similar to Shugoshin-like 2 OS=Homo sapiens PE=2 SV=1 -
	RSF1_HUMAN	Remodeling and spacing factor 1 OS=Homo sapiens GN=RSF1 PE=1 SV=2 -
	K7EPK0_HUMAN	Uncharacterized protein (Fragment) OS=Homo sapiens PE=4 SV=1 -
	PHIP_HUMAN	PH-interacting protein OS=Homo sapiens GN=PHIP PE=1 SV=2 -
	E9PDR3_HUMAN	Voltage-dependent N-type calcium channel subunit alpha-1B OS=Homo sapiens GN=CACNA1B PE=3 SV=3 -
	Q19KS2_HUMAN	Lactoferrin (Fragment) OS=Homo sapiens PE=2 SV=1 -
	Q8TAS6_HUMAN	LAMB1 protein (Fragment) OS=Homo sapiens GN=LAMB1 PE=2 SV=2 -
	CHD6_HUMAN	Chromodomain-helicase-DNA-binding protein 6 OS=Homo sapiens GN=CHD6 PE=1 SV=4 -
	Q53RT9_HUMAN	Putative uncharacterized protein DDEF2 (Fragment) OS=Homo sapiens GN=DDEF2 PE=4 SV=1 -
	B3KS49_HUMAN	cDNA FLJ35478 fis, clone SMINT2007796, highly similar to Gelsolin OS=Homo sapiens PE=2 SV=1 -
	Q6PYX1_HUMAN	Hepatitis B virus receptor binding protein (Fragment) OS=Homo sapiens PE=1 SV=1 -
	ACTH_HUMAN	Actin, gamma-enteric smooth muscle OS=Homo sapiens GN=ACTG2 PE=1 SV=1 -
	Q59GX5_HUMAN	L-plastin variant (Fragment) OS=Homo sapiens PE=2 SV=1 -
	Q08AR5_HUMAN	DNAJC2 protein OS=Homo sapiens GN=DNAJC2 PE=2 SV=1 -

Molar	H7C0W0_HUMAN	Cell differentiation protein RCD1 homolog (Fragment) OS=Homo sapiens GN=RQCD1 PE=1 SV=1 -
	F135A_HUMAN	Protein FAM135A OS=Homo sapiens GN=FAM135A PE=1 SV=2 -
	MORC1_HUMAN	MORC family CW-type zinc finger protein 1 OS=Homo sapiens GN=MORC1 PE=2 SV=2 -
	A0A024R005_HUMAN	Ataxin 1, isoform CRA_c OS=Homo sapiens GN=ATXN1 PE=4 SV=1 -
	B3KWI2_HUMAN	cDNA FLJ43117 fis, clone CTONG3002674, highly similar to Abnormal spindle-like microcephaly-associated protein (Fragment) OS=Homo sapiens PE=2 SV=1 -
	Q8TAK2_HUMAN	Similar to catalase (Fragment) OS=Homo sapiens PE=2 SV=1 -
	A8MX94_HUMAN	Glutathione S-transferase P OS=Homo sapiens GN=GSTP1 PE=1 SV=1 -
	C9JGI3_HUMAN	Thymidine phosphorylase (Fragment) OS=Homo sapiens GN=TYMP PE=1 SV=1 -
	Q6ZNL4_HUMAN	FLJ00279 protein (Fragment) OS=Homo sapiens GN=FLJ00279 PE=2 SV=1 -
	Q5IBP5_HUMAN	AKAP9-BRAF fusion protein OS=Homo sapiens PE=2 SV=1 -
	H2B3B_HUMAN	Histone H2B type 3-B OS=Homo sapiens GN=HIST3H2BB PE=1 SV=3 -
	B7Z2K1_HUMAN	cDNA FLJ54444, highly similar to HECT domain and RCC1-like domain-containing protein 2 OS=Homo sapiens PE=2 SV=1 -
	LCN1_HUMAN	Lipocalin-1 OS=Homo sapiens GN=LCN1 PE=1 SV=1 -
	MUC16_HUMAN	Mucin-16 OS=Homo sapiens GN=MUC16 PE=1 SV=2 -
	B7ZMD7_HUMAN	Alpha-amylase OS=Homo sapiens GN=AMY1A PE=2 SV=1 -
	Q13747_HUMAN	Alpha-1 antitrypsin (Fragment) OS=Homo sapiens PE=2 SV=1 -
	B4DU16_HUMAN	cDNA FLJ54550, highly similar to Homo sapiens fibronectin 1 (FN1), transcript variant 6, mRNA OS=Homo sapiens PE=2 SV=1 -
	A0A087X079_HUMAN	Ig gamma-1 chain C region OS=Homo sapiens GN=IGHG1 PE=1 SV=1 -
	A0A024R9E6_HUMAN	TAF2 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 150kDa, isoform CRA_a OS=Homo sapiens GN=TAF2 PE=4 SV=1 -
	VTDB_HUMAN	Vitamin D-binding protein OS=Homo sapiens GN=GC PE=1 SV=1 -
	FIBB_HUMAN	Fibrinogen beta chain OS=Homo sapiens GN=FGB PE=1 SV=2 -
	D3DP13_HUMAN	Fibrinogen beta chain, isoform CRA_e OS=Homo sapiens GN=FGB PE=4 SV=1 -
	A8K964_HUMAN	cDNA FLJ75071, highly similar to Homo sapiens pinin, desmosome associated protein (PNN), mRNA OS=Homo sapiens PE=2 SV=1 -
	TOP2A_HUMAN	DNA topoisomerase 2-alpha OS=Homo sapiens GN=TOP2A PE=1 SV=3 -
	PDS5B_HUMAN	Sister chromatid cohesion protein PDS5 homolog B OS=Homo sapiens GN=PDS5B PE=1 SV=1 -
	Q9H6H8_HUMAN	Histone-lysine N-methyltransferase OS=Homo sapiens PE=2 SV=1 -
	B7ZBM3_HUMAN	Forkhead box protein P4 OS=Homo sapiens GN=FOXP4 PE=1 SV=1 -
	B4DU58_HUMAN	cDNA FLJ51488, highly similar to Macrophage capping protein OS=Homo sapiens PE=2 SV=1 -
	B4E0Q9_HUMAN	cDNA FLJ52821, highly similar to Protein transport protein Sec23A OS=Homo sapiens PE=2 SV=1 -
	A8K822_HUMAN	cDNA FLJ77778, highly similar to Homo sapiens death-associated protein 6 (DAXX), mRNA OS=Homo sapiens PE=2 SV=1 -
	COF1_HUMAN	Cofilin-1 OS=Homo sapiens GN=CFL1 PE=1 SV=3 -
	B4DNY3_HUMAN	Adenylyl cyclase-associated protein OS=Homo sapiens PE=2 SV=1 -
	PEBP1_HUMAN	Phosphatidylethanolamine-binding protein 1 OS=Homo sapiens GN=PEBP1 PE=1 SV=3 -
	A8K3K1_HUMAN	cDNA FLJ78096, highly similar to Homo sapiens actin, alpha, cardiac muscle (ACTC), mRNA OS=Homo sapiens PE=2 SV=1 -

NOP2_HUMAN	Probable 28S rRNA (cytosine(4447)-C(5))-methyltransferase OS=Homo sapiens GN=NOP2 PE=1 SV=2 -
ANXA5_HUMAN	Annexin A5 OS=Homo sapiens GN=ANXA5 PE=1 SV=2 -
E7ENN3_HUMAN	Nesprin-1 OS=Homo sapiens GN=SYNE1 PE=1 SV=2 -
Q6GMV8_HUMAN	Uncharacterized protein OS=Homo sapiens PE=2 SV=1 -
B4DUI8_HUMAN	cDNA FLJ52761, highly similar to Actin, aortic smooth muscle OS=Homo sapiens PE=2 SV=1 -
B4DMA2_HUMAN	cDNA FLJ54023, highly similar to Heat shock protein HSP 90-beta OS=Homo sapiens PE=2 SV=1 -
WIZ_HUMAN	Protein Wiz OS=Homo sapiens GN=WIZ PE=1 SV=2 -
SRRM4_HUMAN	Serine/arginine repetitive matrix protein 4 OS=Homo sapiens GN=SRRM4 PE=1 SV=2 -
B4DKH3_HUMAN	Activating transcription factor 7-interacting protein 2 OS=Homo sapiens GN=ATF7IP2 PE=1 SV=1 -
B4DL17_HUMAN	cDNA FLJ52558, highly similar to Keratin, type I cytoskeletal 13 OS=Homo sapiens PE=2 SV=1 -
BRWD1_HUMAN	Bromodomain and WD repeat-containing protein 1 OS=Homo sapiens GN=BRWD1 PE=1 SV=4 -
KDM2B_HUMAN	Lysine-specific demethylase 2B OS=Homo sapiens GN=KDM2B PE=1 SV=1 -
W8QEY1_HUMAN	Lactoferrin OS=Homo sapiens PE=2 SV=1 -
A0A0A0MRM9_HUMAN	Nucleolar and coiled-body phosphoprotein 1 (Fragment) OS=Homo sapiens GN=NOLC1 PE=1 SV=1 -
LAMA1_HUMAN	Laminin subunit alpha-1 OS=Homo sapiens GN=LAMA1 PE=1 SV=2 -
B3KPS3_HUMAN	cDNA FLJ32131 fis, clone PEBLM2000267, highly similar to Tubulin alpha-ubiquitous chain OS=Homo sapiens PE=2 SV=1 -
Q96BG6_HUMAN	ACTN4 protein (Fragment) OS=Homo sapiens GN=ACTN4 PE=2 SV=2 -
B4DNV4_HUMAN	cDNA FLJ53071, highly similar to Heat shock 70 kDa protein 1 OS=Homo sapiens PE=2 SV=1 -
CAMP3_HUMAN	Calmodulin-regulated spectrin-associated protein 3 OS=Homo sapiens GN=CAMSAP3 PE=1 SV=2 -
J3KQ66_HUMAN	Reelin OS=Homo sapiens GN=RELN PE=1 SV=1 -
H9KV48_HUMAN	Plasma protease C1 inhibitor OS=Homo sapiens GN=SERPING1 PE=1 SV=1 -
E9PFF2_HUMAN	Transketolase OS=Homo sapiens GN=TKT PE=1 SV=1 -
SPB3_HUMAN	Serpin B3 OS=Homo sapiens GN=SERPINB3 PE=1 SV=2 -
VP13A_HUMAN	Vacuolar protein sorting-associated protein 13A OS=Homo sapiens GN=VPS13A PE=1 SV=2 -
F6QMI7_HUMAN	Dystonin OS=Homo sapiens GN=DST PE=1 SV=2 -
CC168_HUMAN	Coiled-coil domain-containing protein 168 OS=Homo sapiens GN=CCDC168 PE=2 SV=2 -
PGAM1_HUMAN	Phosphoglycerate mutase 1 OS=Homo sapiens GN=PGAM1 PE=1 SV=2 -
SCN3A_HUMAN	Sodium channel protein type 3 subunit alpha OS=Homo sapiens GN=SCN3A PE=1 SV=2 -
Q5H8Y1_HUMAN	Tyrosine-protein kinase receptor OS=Homo sapiens GN=ROS1 PE=3 SV=1 -
B2R835_HUMAN	cDNA, FLJ93721, highly similar to Homo sapiens NADP-dependent retinol dehydrogenase/reductase (RDHL),transcript variant C, mRNA OS=Homo sapiens PE=2 SV=1 -
BRPF1_HUMAN	Peregrin OS=Homo sapiens GN=BRPF1 PE=1 SV=2 -
SETBP_HUMAN	SET-binding protein OS=Homo sapiens GN=SETBP1 PE=1 SV=3 -
1433Z_HUMAN	14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1 -
H0YMM1_HUMAN	Annexin (Fragment) OS=Homo sapiens GN=ANXA2 PE=1 SV=1 -

HV313_HUMAN	Ig heavy chain V-III region POM OS=Homo sapiens PE=1 SV=1 -
A8K2F9_HUMAN	cDNA FLJ77037, highly similar to Homo sapiens RNA polymerase II associated protein 1, mRNA (Fragment) OS=Homo sapiens PE=2 SV=1 -
A0A024R2Y4_HUMAN	Bassoon (Presynaptic cytomatrix protein), isoform CRA_a OS=Homo sapiens GN=BSN PE=4 SV=1 -
B7Z8Q7_HUMAN	cDNA FLJ53871, highly similar to Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens PE=2 SV=1 -
D3DPF9_HUMAN	Titin, isoform CRA_b OS=Homo sapiens GN=TTN PE=4 SV=1 -
C8C504_HUMAN	Beta-globin OS=Homo sapiens GN=HBB PE=3 SV=1 -
B4DTT4_HUMAN	cDNA FLJ54440, weakly similar to Dynamin-binding protein OS=Homo sapiens PE=2 SV=1 -
Q6MZU6_HUMAN	Putative uncharacterized protein DKFZp686C15213 OS=Homo sapiens GN=DKFZp686C15213 PE=2 SV=1 -
MMP9_HUMAN	Matrix metalloproteinase-9 OS=Homo sapiens GN=MMP9 PE=1 SV=3 -
B3KX96_HUMAN	cDNA FLJ45003 fis, clone BRAWH3011623, highly similar to Heterogeneous nuclear ribonucleoproteins C OS=Homo sapiens PE=2 SV=1 -
O75555_HUMAN	ABC transporter MOAT-B isoform (Fragment) OS=Homo sapiens GN=MOAT-B PE=2 SV=1 -
A0A096LPL1_HUMAN	Uncharacterized protein (Fragment) OS=Homo sapiens PE=4 SV=1 -
B4E335_HUMAN	cDNA FLJ52842, highly similar to Actin, cytoplasmic 1 OS=Homo sapiens PE=2 SV=1 -
HECD4_HUMAN	Probable E3 ubiquitin-protein ligase HECTD4 OS=Homo sapiens GN=HECTD4 PE=1 SV=5 -
HBB_HUMAN	Hemoglobin subunit beta OS=Homo sapiens GN=HBB PE=1 SV=2 -
A0A024R609_HUMAN	Pyruvate kinase OS=Homo sapiens GN=PKM2 PE=3 SV=1 -
HSP7C_HUMAN	Heat shock cognate 71 kDa protein OS=Homo sapiens GN=HSPA8 PE=1 SV=1 -
KIF15_HUMAN	Kinesin-like protein KIF15 OS=Homo sapiens GN=KIF15 PE=1 SV=1 -
J3QLC9_HUMAN	Haptoglobin (Fragment) OS=Homo sapiens GN=HP PE=1 SV=1 -
CTRB1_HUMAN	Chymotrypsinogen B OS=Homo sapiens GN=CTRB1 PE=2 SV=1 -
B2R6A9_HUMAN	cDNA, FLJ92868, highly similar to Homo sapiens HIRA interacting protein 3 (HIRIP3), mRNA OS=Homo sapiens PE=2 SV=1 -
ZC3H3_HUMAN	Zinc finger CCCH domain-containing protein 3 OS=Homo sapiens GN=ZC3H3 PE=1 SV=3 -
Q8N355_HUMAN	IGL@ protein OS=Homo sapiens GN=IGL@ PE=1 SV=1 -
E7EW77_HUMAN	Abl interactor 2 OS=Homo sapiens GN=ABI2 PE=1 SV=1 -
B3KUI1_HUMAN	cDNA FLJ39956 fis, clone SPLEN2024990, highly similar to Plastin-2 OS=Homo sapiens PE=2 SV=1 -
A0A024RD92_HUMAN	HCG39854, isoform CRA_a OS=Homo sapiens GN=hCG_39854 PE=4 SV=1 -
ZN281_HUMAN	Zinc finger protein 281 OS=Homo sapiens GN=ZNF281 PE=1 SV=1 -
H2B1K_HUMAN	Histone H2B type 1-K OS=Homo sapiens GN=HIST1H2BK PE=1 SV=3 -
E9M4D4_HUMAN	Hemoglobin alpha-1 globin chain (Fragment) OS=Homo sapiens GN=HBA1 PE=3 SV=1 -
I6L894_HUMAN	Ankyrin-2 OS=Homo sapiens GN=ANK2 PE=1 SV=1 -
F8VY01_HUMAN	FYVE, RhoGEF and PH domain-containing protein 6 OS=Homo sapiens GN=FGD6 PE=1 SV=1 -
H0Y390_HUMAN	Microtubule-actin cross-linking factor 1, isoforms 1/2/3/5 (Fragment) OS=Homo sapiens GN=MACF1 PE=1 SV=1 -
A0A087WVQ9_HUMAN	Elongation factor 1-alpha 1 OS=Homo sapiens GN=EEF1A1 PE=1 SV=1 -
LYSC_HUMAN	Lysozyme C OS=Homo sapiens GN=LYZ PE=1 SV=1 -

FREM1_HUMAN	FRAS1-related extracellular matrix protein 1 OS=Homo sapiens GN=FREM1 PE=1 SV=3 -
MUC5A_HUMAN	Mucin-5AC OS=Homo sapiens GN=MUC5AC PE=1 SV=4 -
B5ME49_HUMAN	Mucin-16 OS=Homo sapiens GN=MUC16 PE=1 SV=2 -
A8K967_HUMAN	cDNA FLJ77623, highly similar to Homo sapiens glutamate decarboxylase 1 (brain, 67kDa) (GAD1), transcript variant GAD67, mRNA OS=Homo sapiens PE=2 SV=1 -
A4QPB0_HUMAN	IQ motif containing GTPase activating protein 1 OS=Homo sapiens GN=IQGAP1 PE=1 SV=1 -
IRS1_HUMAN	Insulin receptor substrate 1 OS=Homo sapiens GN=IRS1 PE=1 SV=1 -
Q6MZV6_HUMAN	Putative uncharacterized protein DKFZp686L19235 OS=Homo sapiens GN=DKFZp686L19235 PE=2 SV=1 -
J3KTF8_HUMAN	Rho GDP-dissociation inhibitor 1 (Fragment) OS=Homo sapiens GN=ARHGDIA PE=1 SV=4 -
B4DR82_HUMAN	cDNA FLJ60331, highly similar to Nicastrin OS=Homo sapiens PE=2 SV=1 -
MTAP2_HUMAN	Microtubule-associated protein 2 OS=Homo sapiens GN=MAP2 PE=1 SV=4 -
E9PN89_HUMAN	Heat shock cognate 71 kDa protein (Fragment) OS=Homo sapiens GN=HSPA8 PE=1 SV=1 -
G3CIG0_HUMAN	MUC19 variant 12 OS=Homo sapiens GN=MUC19 PE=2 SV=1 -

Table 4 describes the function and location of the proteins regarding proteins/peptides found in all groups (n= 19). Single proteins/peptides found in each group individually: No alteration (43), PCO (92), RRR (23), Necrosis (16), Molar (114).

Table 4. Proteins/peptides function and location of groups.

Groups	Entry name	Protein names	Function	Cellular localization
Molar x Necrosis x No Alteration x PCO x RRR	B4DL87_HUMAN	cDNA FLJ52243, highly similar to Heat-shock protein beta-1	(-)	(-)
	F6KPG5_HUMAN	Albumin (Fragment)	(-)	Extracellular region
	BASP1_HUMAN	Brain acid soluble protein 1	Cell differentiation	Plasma membrane
	B4E1T1_HUMAN	cDNA FLJ54081, highly similar to Keratin, type II cytoskeletal 5	Structural components	Cytoskeleton
	HPT_HUMAN	Haptoglobin	Immune response/ cell degradation and recycling/ repair and maintenance	Extracellular region
	B4DWU6_HUMAN	cDNA FLJ51361, highly similar to Keratin, type II cytoskeletal 6A	Structural components	Cytoskeleton
	S10A8_HUMAN	Protein S100-A8	Immune response/ cell degradation and recycling/ repair and maintenance	Plasma membrane / extracellular region / cytoskeleton

	Q71V99_HUMAN	Peptidyl-prolyl cis-trans isomerase	Folding/ enzymatic process	(-)
	B8ZZQ6_HUMAN	Prothymosin alpha	(-)	Cytosol / nucleoplasm
	A2MG_HUMAN	Alpha-2-macroglobulin	Cell differentiation/ cell binding	Extracellular region
	IGKC_HUMAN	Ig kappa chain C region	Immune response	Plasma membrane/ extracellular region
	FIBA_HUMAN	Fibrinogen alpha chain	Immune response	Extracellular region
	ENOA_HUMAN	Alpha-enolase	Enzymatic Process/ Repair and maintenance/ immune response	Plasma membrane / nucleus
	CALL3_HUMAN	Calmodulin-like protein 3	Cell binding	Extracellular region
	B1AN48_HUMAN	Small proline-rich protein 3 (Fragment)	(-)	(-)
	S10A9_HUMAN	Protein S100-A9	Immune response/ cell degradation and recycling/ repair and maintenance	Plasma membrane / extracellular region / cytoskeleton
	TYB4_HUMAN	Thymosin beta-4	Structural components / Cell signaling/ cell migration/ cell signaling	Cytoskeleton
	B4E1B2_HUMAN	cDNA FLJ53691, highly similar to Serotransferrin	Cell binding	Extracellular region
	1433S_HUMAN	14-3-3 protein sigma	Cell degradation and recycling/ cell cycle/ structural components	Extracellular region / nucleus
No alteration	H3BRY3_HUMAN	Coronin	Cell binding	(-)
	B4DXL2_HUMAN	cDNA FLJ58638, highly similar to Homo sapiens Rho GTPase activating protein 28 (ARHGAP28), transcript variant 1, mRNA	Cell signaling	Integral membrane component
	B4E1W5_HUMAN	cDNA FLJ58877, highly similar to FXYD domain-containing ion transport regulator 5	Transporting	Plasma membrane
	Q5T0H8_HUMAN	Gelsolin	Cell binding and contraction	(-)
	RAG1_HUMAN	V(D)J recombination-activating protein 1	Immune response/ cell degradation and recycling	Nucleus
	I6L9F6_HUMAN	NEFL protein	Structural components	Cytoskeleton
	Q5JQ13_HUMAN	Vinculin (Fragment)	(-	(-
	B7Z4I6_HUMAN	cDNA FLJ55581, highly similar to AF4/FMR2 family member 3 (Fragment)	(-)	(-)

DAAM2_HUMAN	Disheveled-associated activator of morphogenesis 2	Cell organization	Extracellular region
PP4R4_HUMAN	Serine/threonine-protein phosphatase 4 regulatory subunit 4	Enzymatic process	Cytoplasm
E9PB13_HUMAN	Kinase suppressor of Ras 2	Enzymatic process/ cell signaling	Intracellular
Q6P1L4_HUMAN	PYGL protein (Fragment)	Enzymatic process	(-)
I3L1U9_HUMAN	Actin, cytoplasmic 2 (Fragment)	(-)	(-)
ATG2B_HUMAN	Autophagy-related protein 2 homolog B	Cell degradation and recycling	Membrane
GLCI1_HUMAN	Glucocorticoid-induced transcript 1 protein	(-)	(-)
GP158_HUMAN	Probable G-protein coupled receptor 158	Cell signaling	Plasma membrane
A0A024QYV8_HUMAN	CP110 protein, isoform CRA_a	Cell cycle	Cytoskeleton
B7ZW05_HUMAN	AKAP13 protein (Fragment)	Enzymatic process	Intracellular
J3KRE2_HUMAN	Rho GDP-dissociation inhibitor 1	Enzymatic process	Cytoplasm
F2Z393_HUMAN	Transaldolase	Enzymatic process	Cytosol
H0YNA1_HUMAN	Protein FAM98B (Fragment)	(-)	(-)
H0YJG4_HUMAN	Chromodomain-helicase-DNA-binding protein 8 (Fragment)	Cell binding	(-)
FSIP2_HUMAN	Fibrous sheath-interacting protein 2	(-)	Mitochondria
PTN12_HUMAN	Tyrosine-protein phosphatase non-receptor type 12	Repair and maintenance/ cell signaling	Cytoplasm
GPTC8_HUMAN	G patch domain-containing protein 8	Cell binding	(-)
F8WA11_HUMAN	CLIP-associating protein 1	Cell binding	Cytoskeleton
T1S9D5_HUMAN	MUC5AC (Fragment)	(-)	(-)
A0AUL6_HUMAN	ACTB protein (Fragment)	(-)	(-)
G3XAK3_HUMAN	CAP-Gly domain-containing linker protein 4	(-)	Integral membrane component
Q8NEY2_HUMAN	Hepatocellular carcinoma-associated antigen	Cell binding	(-)
FAK2_HUMAN	Protein-tyrosine kinase 2-beta	Enzymatic Process/ Repair and maintenance/ immune response	Plasma membrane / nucleus
G3V380_HUMAN	Alpha-actinin-1 (Fragment)	(-)	(-)
TET1_HUMAN	Methylcytosine dioxygenase TET1	Cell differentiation/ cell cycle	Nucleus
B4DHZ6_HUMAN	Transferrin, isoform CRA_c	(-)	Extracellular region
PPR29_HUMAN	Protein phosphatase 1 regulatory subunit 29	Enzymatic process	Plasma membrane
CAP1_HUMAN	Adenylyl cyclase-associated protein 1	Enzymatic process	Plasma membrane
B4DXY3_HUMAN	cDNA FLJ56517, highly similar to Heat shock 70 kDa protein 1L	Cell binding/ repair and maintenance	(-)
J3KPF0_HUMAN	Probable E3 ubiquitin-protein ligase HECTD4	Enzymatic process	(-)

	B4DEF7_HUMAN	cDNA FLJ60062, highly similar to 78 kDa glucose-regulated protein	Cell binding	(-)
	A8K7T1_HUMAN	cDNA FLJ76055, highly similar to Homo sapiens purinergic receptor P2Y, G-protein coupled, 12 (P2RY12), transcript variant 1, mRNA	Cell receptor	Integral membrane component
	NEB2_HUMAN	Neurabin-2	Cell migration/ Cell differentiation/ cell cycle	Plasma membrane / cytoskeleton/ nucleus
	Q86XU5_HUMAN	MYH9 protein (Fragment)	Contraction	Cytoskeleton
	C9JPJ8_HUMAN	Palmitoyltransferase ZDHHC23 (Fragment)	(-)	Integral membrane component
PCO	HS90A_HUMAN	Heat shock protein HSP 90-alpha	Cell cycle	Plasma membrane
	Q96IS6_HUMAN	HSPA8 protein (Fragment)	Cell binding	(-)
	B4E2Y9_HUMAN	cDNA FLJ58668, highly similar to Calreticulin	Folding	Endoplasmic reticulum
	MTA70_HUMAN	N6-adenosine-methyltransferase 70 kDa subunit	Repair and maintenance	Nucleus
	B7Z5V2_HUMAN	cDNA FLJ54141, highly similar to Ezrin	Cell binding	Cytoskeleton
	TEX35_HUMAN	Testis-expressed sequence 35 protein	(-)	Cytoskeleton
	C9JFF0_HUMAN	Kinesin-like protein	Contraction	(-)
	I3L182_HUMAN	Serine/arginine repetitive matrix protein 2 (Fragment)	(-)	Nucleus
	A0A087WUE9_HUMAN	Symplekin	(-)	Cytosol/ plasmatic membrane/ nucleoplasm
	I3NI03_HUMAN	Protein disulfide-isomerase (Fragment)	Enzymatic process	Cellular
	PA24B_HUMAN	Cytosolic phospholipase A2 beta	Enzymatic process / Immune response/ cell signaling	Cytosol
	H7C070_HUMAN	Uncharacterized protein KIAA1109 (Fragment)	(-)	(-)
	H13_HUMAN	Histone H1.3	Structural components/ cell binding	Chromosome/ nucleus
	O60382_HUMAN	KIAA0324 (Fragment)	(-)	(-)
	D6RF92_HUMAN	C-X-C motif chemokine	Immune response	Extracellular region
	ALKB5_HUMAN	RNA demethylase ALKBH5	Repair and maintenance/ cell differentiation	Nucleus
	Q9UQC1_HUMAN	Heat shock protein 72 (Fragment)	Cell binding	(-)
	E9PBD8_HUMAN	Lymphocyte-specific protein 1 (Fragment)	Cell signaling	Membrane
	H2B1B_HUMAN	Histone H2B type 1-B	Repair and maintenance	Chromosome/ nucleus

A0A087X010_HUMAN	Ig gamma-1 chain C region	(-	(-
ADGB_HUMAN	Androglobin	Enzymatic process/ cell binding	Cytoplasm
B4DSX7_HUMAN	cDNA FLJ59047	(-)	(-)
G3V544_HUMAN	Alpha-1-antitrypsin (Fragment)	(-)	Extracellular region
LYSM2_HUMAN	LysM and putative peptidoglycan-binding domain-containing protein 2	(-)	(-)
Q9BYF7_HUMAN	SCCA2b	(-)	Extracellular region
Q53HU8_HUMAN	Vimentin variant (Fragment)	Structural components	Cytoskeleton
Q13707_HUMAN	ACTA2 protein (Fragment)	(-)	(-)
A0A087WWU8_HUMAN	Tropomyosin alpha-3 chain	(-)	(-)
Q53G71_HUMAN	Calreticulin variant (Fragment)	Folding	Endoplasmic reticulum
A0A0C4DFX2_HUMAN	Protein furry homolog	(-)	(-)
A0A087WTR6_HUMAN	Protocadherin-15	Cell adhesion/ cell binding	Plasma membrane
DYH5_HUMAN	Dynein heavy chain 5, axonemal	Enzymatic process/ structural components	Cytoskeleton
B3KPD3_HUMAN	cDNA FLJ31633 fis, clone NT2RI2003407, highly similar to Inner centromere protein (Fragment)	(-)	(-)
A0A0B5HJK3_HUMAN	Truncated ALSM1	Transporting	Intracellular
A0A087WTW5_HUMAN	CASP8-associated protein 2	Enzymatic process/ cell degradation and recycling/ cell signaling	(-)
B4DUT7_HUMAN	cDNA FLJ57604, highly similar to GMP synthase (glutamine-hydrolyzing) (EC 6.3.5.2)	Enzymatic process/ cell binding	(-)
Q5T085_HUMAN	Alpha-amylase (Fragment)	Enzymatic process	(-)
H0YMT1_HUMAN	Talin-2 (Fragment)	Cell adhesion	(-)
E1B2D1_HUMAN	Hemoglobin alpha-1 globin chain variant (Fragment)	Cell binding	Cytosol
A8K6L7_HUMAN	cDNA FLJ78668, highly similar to Homo sapiens deleted in liver cancer 1 (DLC1), transcript variant 1, mRNA	Enzymatic process	(-)
ITPR2_HUMAN	Inositol 1,4,5-trisphosphate receptor type 2	Cell binding/ transporting/ repair and maintenance	Endoplasmic reticulum
E9PJP2_HUMAN	Protein SOGA3	Cell degradation and recycling	Extracellular region
CENPF_HUMAN	Centromere protein F	Cell differentiation/ cycle	Nucleus/ cytoskeleton
B7Z1S3_HUMAN	cDNA FLJ56058, highly similar to Castor homolog 1 zinc finger protein	Cell binding	(-)

B4DSK7_HUMAN	cDNA FLJ50196, highly similar to Peroxisome proliferator-activated receptor-binding protein (Fragment)	Enzymatic process	Nucleus
C9JTX5_HUMAN	Actin, cytoplasmic 1 (Fragment)	(-)	(-)
KRR1_HUMAN	KRR1 small subunit processome component homolog	Cell binding	Nucleus
ZN862_HUMAN	Zinc finger protein 862	Cell binding	Nucleus
Q6ZTL7_HUMAN	cDNA FLJ44537 fis, clone UTERU3005049	(-)	(-)
B7Z9A0_HUMAN	cDNA FLJ56212, highly similar to Gelsolin	Cell binding	(-)
B4E1L9_HUMAN	cDNA FLJ51603	(-)	(-)
HERC2_HUMAN	E3 ubiquitin-protein ligase HERC2	Repair and maintenance	Cytoskeleton
D3DPG0_HUMAN	Titin, isoform CRA_a	Enzymatic process/ cell binding	(-)
TITIN_HUMAN	Titin	Enzymatic process/ cell binding	Nucleus/ cytoplasm
C6KXN3_HUMAN	Lambda light chain of human immunoglobulin surface antigen-related protein (Fragment)	(-	(-
V9HVZ7_HUMAN	Epididymis luminal protein 176	(-)	(-)
FREM2_HUMAN	FRAS1-related extracellular matrix protein 2	Cell adhesion/ communication	Plasma membrane
F8VYN8_HUMAN	Centrosomal protein of 83 kDa	Cell organization	Cytoskeleton
B7Z2E6_HUMAN	14-3-3 protein zeta/delta	Enzymatic process	(-)
Q6B823_HUMAN	Histone H4 (Fragment)	Cell cycle/ repair and maintenance	Nucleus
B4DVG9_HUMAN	cDNA FLJ57007, highly similar to Microtubule-associated protein 9	Cell cycle	(-)
U2AFL_HUMAN	U2 small nuclear ribonucleoprotein auxiliary factor 35 kDa subunit-related protein 1	Cell binding	Nucleus
B2RCA2_HUMAN	cDNA, FLJ95932, Homo sapiens polyamine modulated factor 1 binding protein 1(PMFBP1), mRNA	(-)	(-)
UBR4_HUMAN	E3 ubiquitin-protein ligase UBR4	Enzymatic process	Nucleus/ cytoskeleton
H7C0L5_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H4 (Fragment)	Enzymatic process	(-)
A0A087WV66_HUMAN	Antigen KI-67	(-	(-
LRR70_HUMAN	Leucine-rich repeat-containing protein 70	Immune response	Integral membrane protein
MYLK_HUMAN	Myosin light chain kinase, smooth muscle	Cell degradation and recycling/ repair and maintenance	Cytoskeleton/ cytoplasm
Q53FC7_HUMAN	Heat shock 70kDa protein 6 (HSP70B') variant (Fragment)	Cell binding	(-)

	Q6PEJ8_HUMAN	HP protein	Enzymatic process	(-)
	MYH7B_HUMAN	Myosin-7B	Contraction	Membrane
	YM012_HUMAN	Uncharacterized protein DKFZp434B061	(-)	Extracellular space
	B5MC15_HUMAN	Cas-Br-M (Murine) ecotropic retroviral transforming sequence b, isoform CRA_a	Cell binding/ signaling	Cytosol/ nucleoplasm
	Q1HW68_HUMAN	ADAM21-like protein	Enzymatic process	(-)
	MYCB2_HUMAN	E3 ubiquitin-protein ligase MYCBP2	Enzymatic process	Nucleus
	B4DMJ7_HUMAN	HCG2015269, isoform CRA_c	Enzymatic process	(-)
	Q59FC6_HUMAN	Tumor rejection antigen (Gp96) 1 variant (Fragment)	Repair and maintenance	(-)
	SYTL2_HUMAN	Synaptotagmin-like protein 2	Cell binding/ transporting	Plasma membrane
	S100P_HUMAN	Protein S100-P	Cell cycle/ signaling/ migration	Nucleus/ plasma membrane
	A2BDK6_HUMAN	Microtubule-associated protein 1B	Cell development/ structural components	Cytoskeleton
	E7EVA0_HUMAN	Microtubule-associated protein	Cell binding	Cytoskeleton
	B7WPD9_HUMAN	Kinesin-like protein	Cell binding/ contraction	(-)
	ZN831_HUMAN	Zinc finger protein 831	Cell binding	Nucleus
	ARRS_HUMAN	S-arrestin	Cell signaling	Plasma membrane
	M0QY24_HUMAN	Zinc finger protein 546	Cell binding	(-)
	A8K4M9_HUMAN	cDNA FLJ78738, highly similar to Homo sapiens ankyrin repeat-containing cofactor-1 (ANCO1) mRNA (Fragment)	(-)	(-)
	B4DVU1_HUMAN	cDNA FLJ53217, highly similar to Transketolase (EC 2.2.1.1)	Enzymatic process	(-)
	Q53HF2_HUMAN	Heat shock 70kDa protein 8 isoform 2 variant (Fragment)	Cell binding	(-)
	ALPK2_HUMAN	Alpha-protein kinase 2	Enzymatic process/ cell binding	Cytoplasm
	A0A024RDD6_HUMAN	Uncharacterized protein	(-)	(-)
	CFA58_HUMAN	Cilia- and flagella-associated protein 58	(-)	Cilium
	CATA_HUMAN	Catalase	Enzymatic process/cell differentiation/ repair and maintenance	Peroxisome
RRR	A4D2J6_HUMAN	Phosphoglycerate mutase	Enzymatic process	(-)
	B4DJS0_HUMAN	cDNA FLJ56766, highly similar to Protein disulfide-isomerase (EC5.3.4.1)	Enzymatic process	Cell
	KLH24_HUMAN	Kelch-like protein 24	Cell degradation and recycling/ cell differentiation	Cytoplasm
	I3L312_HUMAN	Protein disulfide-isomerase (Fragment)	(-)	(-)

	CCD96_HUMAN	Coiled-coil domain-containing protein 96	(-)	Cytoskeleton
	Q59GI3_HUMAN	I-kappa-B-related protein variant (Fragment)	(-)	(-)
	H0Y5T1_HUMAN	CLIP-associating protein 1 (Fragment)	Cell binding	Cytoskeleton
	LSP1_HUMAN	Lymphocyte-specific protein 1	Immune response	Plasma membrane
	CALX_HUMAN	Calnexin	Cell signaling/ transporting	Endoplasmic reticulum
	B8ZZF0_HUMAN	Protein phosphatase 1B (Fragment)	Enzymatic process/ cell binding	(-)
	A1YBP1_HUMAN	Breast and ovarian cancer susceptibility protein 2 truncated variant	Repair and maintenance	(-)
	F8VZU9_HUMAN	Myosin light polypeptide 6	Cell binding	(-)
	CC162_HUMAN	Coiled-coil domain-containing protein 162	(-)	(-)
	Q2F831_HUMAN	Tyrosine 3-monooxygenasea/tryptophan 5-monooxygenase activation protein zeta (Fragment)	Enzymatic process/ cell binding	(-)
	B0AZU6_HUMAN	cDNA, FLJ79536, highly similar to Heat shock 70 kDa protein 4	(-)	(-)
	Q7RTM4_HUMAN	Spectrin-like protein of the nuclear envelope and Golgi	Structural components	Nucleus
	FBP12_HUMAN	Fatty acid-binding protein 12	Enzymatic process	Cytosol
	A0A087WWT3_HUMAN	Serum albumin	(-)	Extracellular region
	B4DWQ5_HUMAN	cDNA FLJ51655, highly similar to Actin-like protein 2	Cell binding	Cytoskeleton
	K7EMV3_HUMAN	Histone H3	Cell binding	Nucleus
	H9A532_HUMAN	BCL6 corepressor-cyclin B3 fusion protein	(-)	Nucleus
	KMT2D_HUMAN	Histone-lysine N-methyltransferase 2D	Cell cycle / signaling	Nucleus
	B7Z565_HUMAN	cDNA FLJ54739, highly similar to Alpha-actinin-1	Contraction	(-)
Fistula	C9JN07_HUMAN	HEPACAM family member 2	(-)	Integral component of membrane
	B4DT36_HUMAN	cDNA FLJ60876, highly similar to Semaphorin-6B	(-)	(-)
	B7Z7S9_HUMAN	cDNA FLJ61724, highly similar to Shugoshin-like 2	Cell cycle	Chromosome
	RSF1_HUMAN	Remodeling and spacing factor 1	Cell binding	Nucleus
	K7EPK0_HUMAN	Uncharacterized protein (Fragment)	(-)	(-)
	PHIP_HUMAN	PH-interacting protein	Cell degradation and recycling/ cell cycle	Nucleus
	E9PDR3_HUMAN	Voltage-dependent N-type calcium channel subunit alpha-1B	Cell degradation and recycling/ contraction	Plasma membrane
	Q19KS2_HUMAN	Lactoferrin (Fragment)	Immune response	Extracellular region
	Q8TAS6_HUMAN	LAMB1 protein (Fragment)	(-)	(-)

	CHD6_HUMAN	Chromodomain-helicase-DNA-binding protein 6	Enzymatic process/ repair and maintenance	Nucleus
	Q53RT9_HUMAN	Putative uncharacterized protein DDEF2 (Fragment)	(-)	(-)
	B3KS49_HUMAN	cDNA FLJ35478 fis, clone SMINT2007796, highly similar to Gelsolin	Cell binding	(-)
	Q6PYX1_HUMAN	Hepatitis B virus receptor binding protein (Fragment)	(-)	(-)
	ACTH_HUMAN	Actin, gamma-enteric smooth muscle	Structural components / contraction	Cytoskeleton
	Q59GX5_HUMAN	L-plastin variant (Fragment)	Cell binding	(-)
	Q08AR5_HUMAN	DNAJC2 protein	Cell binding	Nucleus
Molar	H7C0W0_HUMAN	Cell differentiation protein RCD1 homolog (Fragment)	Enzymatic process	(-)
	F135A_HUMAN	Protein FAM135A	Enzymatic process	(-)
	MORC1_HUMAN	MORC family CW-type zinc finger protein 1	Cell differentiation	Nucleus
	A0A024R005_HUMAN	Ataxin 1, isoform CRA_c	Cell binding	(-)
	B3KWI2_HUMAN	cDNA FLJ43117 fis, clone CTONG3002674, highly similar to Abnormal spindle-like microcephaly-associated protein (Fragment)	Structural components	(-)
	Q8TAK2_HUMAN	Similar to catalase (Fragment)	Enzymatic process/ repair and maintenance	(-)
	A8MX94_HUMAN	Glutathione S-transferase P	Enzymatic process	(-)
	C9JGI3_HUMAN	Thymidine phosphorylase (Fragment)	Enzymatic process	(-)
	Q6ZNL4_HUMAN	FLJ00279 protein (Fragment)	Contraction	Cytoskeleton
	Q5IBP5_HUMAN	AKAP9-BRAF fusion protein	Enzymatic process/ cell binding	(-)
	H2B3B_HUMAN	Histone H2B type 3-B	Repair and maintenance	Nucleus
	B7Z2K1_HUMAN	cDNA FLJ54444, highly similar to HECT domain and RCC1-like domain-containing protein 2	Enzymatic process	(-)
	LCN1_HUMAN	Lipocalin-1	Cell binding	Extracellular region
	MUC16_HUMAN	Mucin-16	Immune response	Plasma membrane / extracellular region
	B7ZMD7_HUMAN	Alpha-amylase	Enzymatic process	(-)
	Q13747_HUMAN	Alpha-1 antitrypsin (Fragment)	(-)	Extracellular region
	B4DU16_HUMAN	cDNA FLJ54550, highly similar to Homo sapiens fibronectin 1 (FN1), transcript variant 6, mRNA	(-)	Extracellular region
	A0A087X079_HUMAN	Ig gamma-1 chain C region	(-	(-

A0A024R9E6_HUMAN	TAF2 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 150kDa, isoform CRA_a	(-)	Nucleus
VTDB_HUMAN	Vitamin D-binding protein	Transporting	Extracellular region
FIBB_HUMAN	Fibrinogen beta chain	Immune response	Extracellular region
D3DP13_HUMAN	Fibrinogen beta chain, isoform CRA_e	Repair and maintenance	Extracellular region
A8K964_HUMAN	cDNA FLJ75071, highly similar to Homo sapiens pinin, desmosome associated protein (PNN), mRNA	(-)	(-)
TOP2A_HUMAN	DNA topoisomerase 2-alpha	Cell degradation and recycling	Nucleus
PDS5B_HUMAN	Sister chromatid cohesion protein PDS5 homolog B	Cell cycle	Nucleus
Q9H6H8_HUMAN	Histone-lysine N-methyltransferase	Enzymatic process	Nucleus
B7ZBM3_HUMAN	Forkhead box protein P4	Cell binding	Nucleus
B4DU58_HUMAN	cDNA FLJ51488, highly similar to Macrophage capping protein	Cell binding	(-)
B4E0Q9_HUMAN	cDNA FLJ52821, highly similar to Protein transport protein Sec23A	Transporting	Endoplasmic reticulum
A8K822_HUMAN	cDNA FLJ77778, highly similar to Homo sapiens death-associated protein 6 (DAXX), mRNA	(-)	(-)
COF1_HUMAN	Cofilin-1	Cell migration/ Cell degradation and recycling	Plasma membrane / cytoskeleton/ nucleus
B4DNY3_HUMAN	Adenylyl cyclase-associated protein	Structural components	(-)
PEBP1_HUMAN	Phosphatidylethanolamine-binding protein 1	Enzymatic process	Cytoplasm
A8K3K1_HUMAN	cDNA FLJ78096, highly similar to Homo sapiens actin, alpha, cardiac muscle (ACTC), mRNA	Cell migration	Cytoplasm
NOP2_HUMAN	Probable 28S rRNA (cytosine(4447)-C(5))-methyltransferase	Cell cycle	Nucleus
ANXA5_HUMAN	Annexin A5	Cell degradation and recycling/repair and maintenance	Cytosol / extracellular region
E7ENN3_HUMAN	Nesprin-1	Cell binding	Nucleus
Q6GMV8_HUMAN	Uncharacterized protein	(-)	(-)
B4DUI8_HUMAN	cDNA FLJ52761, highly similar to Actin, aortic smooth muscle	Cell binding	(-)
B4DMA2_HUMAN	cDNA FLJ54023, highly similar to Heat shock protein HSP 90-beta	Folding/ repair and maintenance	(-)
WIZ_HUMAN	Protein Wiz	Cell cycle	Nucleus
SRRM4_HUMAN	Serine/arginine repetitive matrix protein 4	Cell differentiation	Nucleus

B4DKH3_HUMAN	Activating transcription factor 7-interacting protein 2	(-)	(-)
B4DL17_HUMAN	cDNA FLJ52558, highly similar to Keratin, type I cytoskeletal 13	Structural components	Cytoskeleton
BRWD1_HUMAN	Bromodomain and WD repeat-containing protein 1	Structural components	Nucleus
KDM2B_HUMAN	Lysine-specific demethylase 2B	Cell cycle/ repair and maintenance	Nucleus
W8QEY1_HUMAN	Lactoferrin	Immune response	Extracellular region
A0A0A0MRM9_HUMAN	Nucleolar and coiled-body phosphoprotein 1 (Fragment)	(-)	Nucleus
LAMA1_HUMAN	Laminin subunit alpha-1	Cell adhesion/ signaling/ cell development	Extracellular region
B3KPS3_HUMAN	cDNA FLJ32131 fis, clone PEBLM2000267, highly similar to Tubulin alpha-ubiquitous chain	Structural components	Cytoskeleton
Q96BG6_HUMAN	ACTN4 protein (Fragment)	Cell binding	(-)
B4DNV4_HUMAN	cDNA FLJ53071, highly similar to Heat shock 70 kDa protein 1	Cell binding	(-)
CAMP3_HUMAN	Calmodulin-regulated spectrin-associated protein 3	Cell adhesion/ structural components/ cell development	Cytoskeleton
J3KQ66_HUMAN	Reelin	Cell development	(-)
H9KV48_HUMAN	Plasma protease C1 inhibitor	Repair and maintenance	Extracellular region
E9PFF2_HUMAN	Transketolase	(-)	(-)
SPB3_HUMAN	Serpin B3	Enzymatic process/ cell cycle	Cytoplasm
VP13A_HUMAN	Vacuolar protein sorting-associated protein 13A	Cell degradation and recycling/ cell development	Cytosol
F6QMI7_HUMAN	Dystonin	Cell binding	Cytoskeleton
CC168_HUMAN	Coiled-coil domain-containing protein 168	(-)	(-)
PGAM1_HUMAN	Phosphoglycerate mutase 1	Enzymatic process	Cytosol / extracellular region
SCN3A_HUMAN	Sodium channel protein type 3 subunit alpha	Transporting	Plasma membrane
Q5H8Y1_HUMAN	Tyrosine-protein kinase receptor	Enzymatic process	Integral component of membrane
B2R835_HUMAN	cDNA, FLJ93721, highly similar to Homo sapiens NADP-dependent retinol dehydrogenase/reductase (RDHL),transcript variant C, mRNA	(-)	(-)
BRPF1_HUMAN	Peregrin	Cell binding/ signaling	Nucleus
SETBP_HUMAN	SET-binding protein	Cell binding/ enzymatic process	Nucleus

1433Z_HUMAN	14-3-3 protein zeta/delta	Cell degradation and recycling	Cytoplasm
H0YMM1_HUMAN	Annexin (Fragment)	Cell binding/ enzymatic process	(-)
HV313_HUMAN	Ig heavy chain V-III region POM	Immune response	Plasma membrane / extracellular region
A8K2F9_HUMAN	cDNA FLJ77037, highly similar to Homo sapiens RNA polymerase II associated protein 1, mRNA (Fragment)	(-)	(-)
A0A024R2Y4_HUMAN	Bassoon (Presynaptic cytomatrix protein), isoform CRA_a	Cell binding/ transporting	Membrane
B7Z8Q7_HUMAN	cDNA FLJ53871, highly similar to Inter-alpha-trypsin inhibitor heavy chain H4	(-)	(-)
D3DPF9_HUMAN	Titin, isoform CRA_b	Cell binding/ enzymatic process	(-)
C8C504_HUMAN	Beta-globin	Cell binding	Cytosol
B4DTT4_HUMAN	cDNA FLJ54440, weakly similar to Dynamin-binding protein	Cell signaling	Cytoplasm
Q6MZU6_HUMAN	Putative uncharacterized protein DKFZp686C15213	(-)	(-)
MMP9_HUMAN	Matrix metalloproteinase-9	Enzymatic process/ Cell degradation and recycling/ cell signaling/ cell differentiation	Extracellular region
B3KX96_HUMAN	cDNA FLJ45003 fis, clone BRAWH3011623, highly similar to Heterogeneous nuclear ribonucleoproteins C	Cell binding	(-)
O75555_HUMAN	ABC transporter MOAT-B isoform (Fragment)	Enzymatic process/ contraction	Integral component of membrane
A0A096LPL1_HUMAN	Uncharacterized protein (Fragment)	(-	(-
B4E335_HUMAN	cDNA FLJ52842, highly similar to Actin, cytoplasmic 1	Cell binding	(-)
HECD4_HUMAN	Probable E3 ubiquitin-protein ligase HECTD4	Enzymatic process	(-)
HBB_HUMAN	Hemoglobin subunit beta	Cell degradation and recycling/ repair and maintenance/ transporting	Cytosol / extracellular region
A0A024R609_HUMAN	Pyruvate kinase	Enzymatic process	(-)
HSP7C_HUMAN	Heat shock cognate 71 kDa protein	Repair and maintenance/ cell cycle/ folding	Plasma membrane
KIF15_HUMAN	Kinesin-like protein KIF15	Immune response/ contraction	Cytoskeleton
J3QLC9_HUMAN	Haptoglobin (Fragment)	Cell binding	Extracellular region

CTRB1_HUMAN	Chymotrypsinogen B O	Enzymatic process	Extracellular region
B2R6A9_HUMAN	cDNA, FLJ92868, highly similar to Homo sapiens HIRA interacting protein 3 (HIRIP3), mRNA	(-)	(-)
ZC3H3_HUMAN	Zinc finger CCCH domain-containing protein 3	Cell binding/ enzymatic process	Nucleus
Q8N355_HUMAN	IGL@ protein	(-)	(-)
E7EW77_HUMAN	Abl interactor 2	Contraction	(-)
B3KUI1_HUMAN	cDNA FLJ39956 fis, clone SPLEN2024990, highly similar to Plastin-2	(-)	(-)
A0A024RD92_HUMAN	HCG39854, isoform CRA_a	(-)	(-)
ZN281_HUMAN	Zinc finger protein 281	Cell differentiation	Nucleus
H2B1K_HUMAN	Histone H2B type 1-K	Immune response	Nucleus
E9M4D4_HUMAN	Hemoglobin alpha-1 globin chain (Fragment)	Transporting	Cytosol
I6L894_HUMAN	Ankyrin-2	Cell signaling	Plasma membrane
F8VY01_HUMAN	FYVE, RhoGEF and PH domain-containing protein 6	Enzymatic process	(-)
H0Y390_HUMAN	Microtubule-actin cross-linking factor 1, isoforms 1/2/3/5 (Fragment)	Cell binding	Cytoskeleton
A0A087WVQ9_HUMAN	Elongation factor 1-alpha 1	Enzymatic process/ cell binding	(-)
LYSC_HUMAN	Lysozyme C	Immune response	Extracellular region
FREM1_HUMAN	FRAS1-related extracellular matrix protein 1	Cell differentiation	Extracellular region
MUC5A_HUMAN	Mucin-5AC	Immune response	Extracellular region
B5ME49_HUMAN	Mucin-16	Immune response	Plasma membrane
A8K967_HUMAN	cDNA FLJ77623, highly similar to Homo sapiens glutamate decarboxylase 1 (brain, 67kDa) (GAD1), transcript variant GAD67, mRNA	Enzymatic process	(-)
A4QPB0_HUMAN	IQ motif containing GTPase activating protein 1	Enzymatic process	(-)
IRS1_HUMAN	Insulin receptor substrate 1	Cell cycle/ transporting	Cytosol / nucleus / plasma membrane
Q6MZV6_HUMAN	Putative uncharacterized protein DKFZp686L19235	(-)	(-)
J3KTF8_HUMAN	Rho GDP-dissociation inhibitor 1 (Fragment)	Enzymatic process	Cytoplasm
B4DR82_HUMAN	cDNA FLJ60331, highly similar to Nicastrin	Enzymatic process	Integral component of membrane
MTAP2_HUMAN	Microtubule-associated protein 2	Cell development	Cytoskeleton
E9PN89_HUMAN	Heat shock cognate 71 kDa protein (Fragment)	Cell binding	(-)

	G3CIG0_HUMAN	MUC19 variant 12	Immune response	Extracellular region

The overall comparison (Molar x Necrosis x No Alteration x PCO x RRR groups) revealed the following peptides/proteins functions: immune response/cell degradation and recycling/ repair and maintenance/ enzymatic process/ cell binding/ cell signaling/ cell differentiation/ cell migration/ structural components/ antioxidant activity.

In relation to each group individually some proteins were highlighted: Proteins related to apoptotic and/or autophagy process: all groups – S10A8_HUMAN, S10A9_HUMAN, 1433S_HUMAN; no alteration group – RAG1_HUMAN, ATG2B_HUMAN; PCO group – A0A087WTW5_HUMAN, MYLK_HUMAN, E9PJP2_HUMAN; PN group – PHIP_HUMAN; molar group – TOP2A_HUMAN, COF1_HUMAN, ANXA5_HUMAN, KDM2B_HUMAN, 1433Z_HUMAN, VP13A_HUMAN.

Proteins related to reactive oxygen species (ROS) and oxidative stress: all groups – S10A8_HUMAN, S10A9_HUMAN, HPT_HUMAN; group no alteration – FAK2_HUMAN; group PCO – I3NI03_HUMAN; group RRR – B4DJS0_HUMAN, Q2F831_HUMAN; PN group – CHD6_HUMAN; group molar – Q8TAK2_HUMAN, MMP9_HUMAN, HBB_HUMAN.

Proteins associated to actin: all groups – TYB4_HUMAN; no alteration group – H3BRY3_HUMAN, Q5T0H8_HUMAN, DAAM2_HUMAN, CAP1_HUMAN, NEB2_HUMAN; PCO group – B7Z5V2_HUMAN, B7Z9A0_HUMAN; RRR group – B4DWQ5_HUMAN, B7Z565_HUMAN; PN group – B3KS49_HUMAN, ACTH_HUMAN, Q59GX5_HUMAN; molar group – B4DU58_HUMAN, E7ENN3_HUMAN, E7EW77_HUMAN.

Of these 436 single proteins/peptides, only 11 (2.52%) were uncharacterized proteins (Table 5). One of 11 protein/peptides was in the comparison Molar x No Alteration x PCO x RRR groups; three in the comparison No Alteration x PCO groups; one in PCO group; two in PN group; four in Molar group. A0A096LPL1_HUMAN is an Uncharacterized protein that is obsolete in UniProt.

Table 5. Uncharacterized proteins.

Entry name	Protein names
Q8WVW5_HUMAN	Putative uncharacterized protein (Fragment) OS=Homo sapiens PE=2 SV=1 -
Q53RT9_HUMAN	Putative uncharacterized protein DDEF2 (Fragment) OS=Homo sapiens GN=DDEF2 PE=4 SV=1 -
Q6MZU6_HUMAN	Putative uncharacterized protein DKFZp686C15213 OS=Homo sapiens GN=DKFZp686C15213 PE=2 SV=1 -
Q6MZV6_HUMAN	Putative uncharacterized protein DKFZp686L19235 OS=Homo sapiens GN=DKFZp686L19235 PE=2 SV=1 -
K7EPK0_HUMAN	Uncharacterized protein (Fragment) OS=Homo sapiens PE=4 SV=1 -
A0A096LPL1_HUMAN	Uncharacterized protein (Fragment) OS=Homo sapiens PE=4 SV=1 -
YM012_HUMAN	Uncharacterized protein DKFZp434B061 OS=Homo sapiens PE=2 SV=2 -
H7C070_HUMAN	Uncharacterized protein KIAA1109 (Fragment) OS=Homo sapiens GN=KIAA1109 PE=1 SV=1 -
K1210_HUMAN	Uncharacterized protein KIAA1210 OS=Homo sapiens GN=KIAA1210 PE=2 SV=3 -
A0A024RDD6_HUMAN	Uncharacterized protein OS=Homo sapiens GN=LOC285513 PE=4 SV=1 -
Q6GMV8_HUMAN	Uncharacterized protein OS=Homo sapiens PE=2 SV=1 -

5 DISCUSSION

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The preschoolers' parents are not always aware of TDI, and sometimes, even in the event of a light bleeding, they decide it as irrelevant (Odersjö et al. 2018). Many times, the family just know about the TDI when dentist shows the tooth discoloration. That information corroborates with the present study, in which 62,5% of children's parents neither know about TDI nor when dental trauma happened. TDI sequelae can be noxious for both primary and permanent teeth. Concerning to primary tooth sequelae, clinical signal and symptoms can appear after six months up to two years (Qassem et al. 2015; Lauridsen et al. 2017b, 2017a). Those consequences can be tooth discoloration, PCO, RRR, infection-related resorption, ankylosis-related resorption, and premature tooth loss (Qassem et al. 2015; Lauridsen et al. 2017c, 2017b, 2017a). Because the bud of permanent tooth is anatomically close to the apex of primary tooth, the sequelae on permanent tooth will be more severe following primary tooth intrusion and avulsion (Lenzi et al. 2015). Permanent tooth sequelae can be crown dilaceration, odontoma-like, partial or complete arrest of root, enamel hypoplasia and root dilacerations (Kramer et al. 2016). The most suitable TDI treatment procedures are clinical and radiographic following-up, aiming to decrease disturbances in traumatized primary teeth and in their permanent successors (Skaare and Jacobsen 2005; Lenzi et al. 2015). The radiograph exam still has some obstacles to overcome as: problems with dimensions and anatomical superimposition, some distortions of the real size and position, and exposure to radiation (Kereshanan et al. 2008).

In this context, it is time to associate the use of high level methodologies of 21rst Century to improve the diagnosis and prognostic assessment for Healthy Science. Molecular biology has been largely studied to find biomarkers which will help in characterizing either the presence or absence of sickness (Strimbu and Tavel 2010). The main goal of biomarkers use is to aid in diagnosis to broaden resources for disease treatments (Strimbu and Tavel 2010). To obtain such biomarkers, it is necessary to collect fluid or tissue from a healthy or sick subject. GCF is an appropriate fluid to evaluate the relation between periodontal tissues and pulp (Awawdeh et al. 2002). Moreover, the compounds of this fluid will depend on either the health or inflammation

level of periodontal tissues (Kereshanan et al. 2008). GCF is a complex fluid derived from serum with defense cells, structural cells, and oral bacteria, which has the function of preserving and keeping the junctional epithelium and antimicrobial defense of periodontal tissue (Sanara et al. 2015). Furthermore, many host defense cells and proteins may have important function when the tissue is injured (Stashenko et al. 1998; Nair 2004; Sanara et al. 2015). These proteins include: antigen, antibody, cytokines, enzymes, and tissue degradation products, which may have potential for serving as biomarkers of diseases, healing process, and homeostasis (Stashenko et al. 1998; Nair 2004; Sanara et al. 2015). Therefore, collection of GCF is a suitable tool to looking for biomarkers.

To find the dental trauma signature, it was important to gather similar clinical and radiographic features to characterize the groups. GCF is the transmitter of several protein signaling and will bring information about what is happening in the tooth. In other words, dental structures are interconnected into the alveolus: pulp tissue and periodontium, making the GCF an important ally. Therefore, the present study aimed to correlate traumatized primary teeth with specific biomarkers, which could lead to the early prognosis and treatment to reduce the sequelae on the primary and permanent teeth. Thus, the comparison of all groups (Molar x Necrosis x No Alteration x PCO x RRR) revealed that the common peptides/proteins have the main functions related to immune response, cell recycling, repair and maintenance, enzymatic process, cell differentiation, structural components, and antioxidant activity. Those features can be characterized as metabolism and homeostasis. In other words, metabolism are all body reactions to give elements and energy for the body to work (Pornputtapong et al. 2015). And homeostasis refers to process to maintain the body stability, dealing with and responding to any conditions that disturbs this balance (Cannon 1929).

Moreover, its known that autophagy and apoptosis are components that belong to homeostatic process (Kerr et al. 1972). In accordance to this fact, each group presented proteins related to apoptosis, except RRR group. However, 3 peptides/proteins belonged to all groups and correlated to autophagy and/or apoptosis. Thus, all groups presented this homeostatic process pertinent to human body. Reactive oxygen species (ROS) and oxidative stress proteins were found in the groups, ranging from the healthier (molar group) to the most damaged (PN group). Then it is advisable to analyze oxidative responses as well as metabolic and damage

responses because ROS is released from regular mitochondrial metabolism, can react with almost all composites, and its accumulation (named oxidative stress) could damage tissues (Forman et al. 2004; Navarro-Yepes et al. 2014). Notwithstanding, oxidative stress can induce not only damage as apoptosis and cell death, but also responses as transformation, adaptation and repair (Forman et al. 2004; Navarro-Yepes et al. 2014). It is worth highlighting the proteins representative of actin, which are related to several metabolism process as: migration, signaling, endocytosis, cell motility, cellular morphogenesis, cell division, adhesion, cytokinesis, polarized growth, and cell migration (Janji et al. 2006; Gandhi and Goode 2013; Subramanian et al. 2013; Blanchoin et al. 2014). Therefore, all those cellular activities are in accordance to homeostatic process.

The Molar group was defined as control group because is a healthy tooth without previous trauma and rhizolysis. Matrix metalloproteinase-9 (MMP-9) was found in molar group, and metalloproteinases family performed both healthy and inflammation course (Rouet-Benzineb et al. 1999). It is important to have proteins related to inflammation because the oral environment is hostile, which is settle bacteria, virus, fungus, and food debris. Therefore, MMP-9 role in signaling homeostasis. Furthermore, molar group showed 114 peptide/protein, which are playing role in homeostasis process to maintain all periodontal and dental tissues healthy. Describing in minutia, those 114 peptides/proteins functions are relating to homeostasis, metabolism, cellular differentiation, catabolism, cell proliferation, apoptotic process, immune response – bacteriolytic and protective response and oxygen carriers.

Anatomically, each tooth has nerves and blood vessels, which has sensors, receive nutrients, and remove waste. After dental trauma, these nerves and blood vessels can be damaged. Taking into consideration this presumable trauma consequence, in the no alteration group, the probable response was repair or regeneration. Thus, some proteins from no alteration group are related to neurons: I6L9F6_HUMAN (Neurofilament light - NFL) – protein localized in axonal neurons and reported to be a potential biomarker for brain injuries (Shahim et al. 2016, 2017); NEB2_HUMAN (neurabin II – gene PPP1R9B) – related to neuronal migration and dendritic formation (Tsukada et al. 2003); Q5T0H8_HUMAN (Gelsolin) – related to remyelination (Tanaka and Sobue 1994); and H0YJG4_HUMAN (CDH8) related to neuron development (Wilkinson et al. 2015). All these proteins related to nervous

tissue can perform a line of events. Starting to trauma signaling, followed by dendritic and myelinization repair, and concluding with neuron development/regeneration. Moreover, TET1_HUMAN protein was found in pulpal tissue and its related to odontoblast differentiation (Li et al. 2018). It is a significant relation because in dental injury some odontoblast will be damage and this protein maybe will stimulate repair.

Kumar and coworkers (2013) searched for a possible biomarker signaling after TDI and before the radiographic exam shows an apical resorption. This remarkable protein is named by dentine sialoprotein (DSP), which is released and found in GCF in the event of root resorption through enzyme-linked immunosorbent assay (ELISA) to target one or more specific proteins (Kumar et al. 2013). In the present study, DSP was not found probably because the methodological approach - mass spectrometry - cannot detect less abundant protein (Peng et al. 2003). We use mass spectrometry aiming to catalogue TDI profile in deciduous dentition. Moreover, there will be rhizolysis in primary tooth anyhow, and DSP will be released in this physiological process, as seen in Kumar et al. (2013). Therefore, in deciduous dentition is more accurate to consider other proteins than DSP. Three proteins were found in RRR group, as CALX_HUMAN, B8ZZF0_HUMAN, and KMT2D_HUMAN. The first two are related to aging. Studies suggest that lower levels of calnexin (CALX_HUMAN) and protein phosphatase 1B (B8ZZF0_HUMAN) are associated to senescence (Choi and Kim 2004; Naidoo 2009; Park et al. 2014). KMT2D_HUMAN mutation is related to a syndrome that had intrinsic relation with skeletal deformation (Haanpää et al. 2017; Topa et al. 2017). Based on this information, maybe, those proteins are related to an senescence process. Therefore, further studies are necessary to verify a correlation among those proteins and faster resorption in RRR group, because traumatized tooth may undergo faster resorption than a tooth without any injury or trauma (Lauridsen et al. 2017b).

The occurrence of partial damage of neurovascular bundles results in temporary hypoxia and reduces nutrients and cell metabolism (Consolaro and Bernardini 2007). An adaptation mechanism called cellular metaplasia will happen to make the cells survive to this event (Consolaro and Bernardini 2007). This process will conduct fibroblasts and some mesenchymal-like cells to differentiate into odontoblast, leading to a randomized and disorganized production of poorly mineralized dentin, named dysplastic dentin (Consolaro and Bernardini 2007). Three months after trauma, it is

possible to observe an undefined pulp canal limit, and 6 months to 1 year, entire pulp obliteration may take place (Consolaro and Bernardini 2007). Clinically, those teeth show discoloration ranging from yellow to severe darkening (Consolaro and Bernardini 2007). PCO group shows the following proteins: CATA_HUMAN (catalase), which functions are response to hypoxia, transformation of fibroblast cells, and osteoblast differentiation; MTA70_HUMAN protein responsible for regulation of hematopoietic stem cell differentiation; and ITPR2_HUMAN protein stimuli releasing of sequestered calcium ion into cytosol. Maybe those proteins can be related to pulp calcification.

Finally, one of the pulp sequelae can be PN (Lauridsen et al. 2017a, 2017c, 2017b). One consequence of PN can be color change. It was shown that 28% of grey discoloration has sign of bacterial infection and it is advisable to follow-up the traumatized tooth at every 6 months if the discoloration remains (Lauridsen et al. 2017a). In the present study just one tooth (8.30%) had greyish discoloration and fistula. There were more 4 (33.3%) greyish to dark discoloration of teeth that did not have fistula. Around four years-old, PN is at high risk because the apical foramen is enlarged again due to the physiological root resorption process, consequently leading to an easier bacterial access (Lauridsen et al. 2017a). Thus, microorganisms will reach the pulp and root canal and some antigenic microorganisms will release contaminants into the periapex (Nair 2004). Therefore, the junction between bacterial antigenic factors and host defense will cause periapical tissue impairment (Nair 2004). Even with host defense, this lesion will not heal by itself, and endodontic treatment is necessary (Nair 2004).

The following proteins were found in fistula group: Q8TAS6_HUMAN (LAMB1) is associated with development of neuronal tissue (Kim et al. 2015); E9PDR3_HUMAN (Cav2.2) protein reveals to be correlated to neurotransmitter release, cell division and cell death (Gandini et al. 2014). B4DT36_HUMAN (Semaphorin-6B) protein is a member of semaphorins family and plays a role in conducting axon (Correa et al. 2001; Collet et al. 2004). C9JN07_HUMAN protein (HEPACAM family member 2, also known as Miki – mitotic kinetics regulator) is associated to mitotic process, specifically in prometaphase, which is a stage before metaphase (Ozaki et al. 2012). RSF1_HUMAN is an important protein for DNA repair, which if not performed, can lead to apoptosis and senescence (Pessina and Lowndes 2014); Q19KS2_HUMAN (Lactoferrin) is the first line defense, the function is to present the pathogen to adaptive immune defense

(Actor et al. 2009). Taking into accounting these proteins' functions, apparently, they are involved in a process to surround the infection/inflammation site.

The limitation of this present study was the number of injured teeth and the cross-sectional assessment. Further longitudinal studies are necessary to follow-up TDI since its onset until the exfoliation, in order to find the functionality of these proteins, in different stages of TDI. Due to the exfoliation process, more studies on TDI in primary dentition are necessary because the proteins may be different from those of TDI in permanent tooth. In summary, the proteins found in each group play a characteristic role in the cellular process.

6 CONCLUSION

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The TDI profile of primary tooth undergoing different sequelae type was characterized. The proteins of molar group exhibited complete homeostasis. In no alteration group, the proteins play a role in maintaining the nervous tissue. The proteins of PCO group were involved in cell transformation and differentiation to reach canal root obliteration. The proteins of RRR group revealed a senescence process. In fistula group the proteins play a role to surround the inflammation site.

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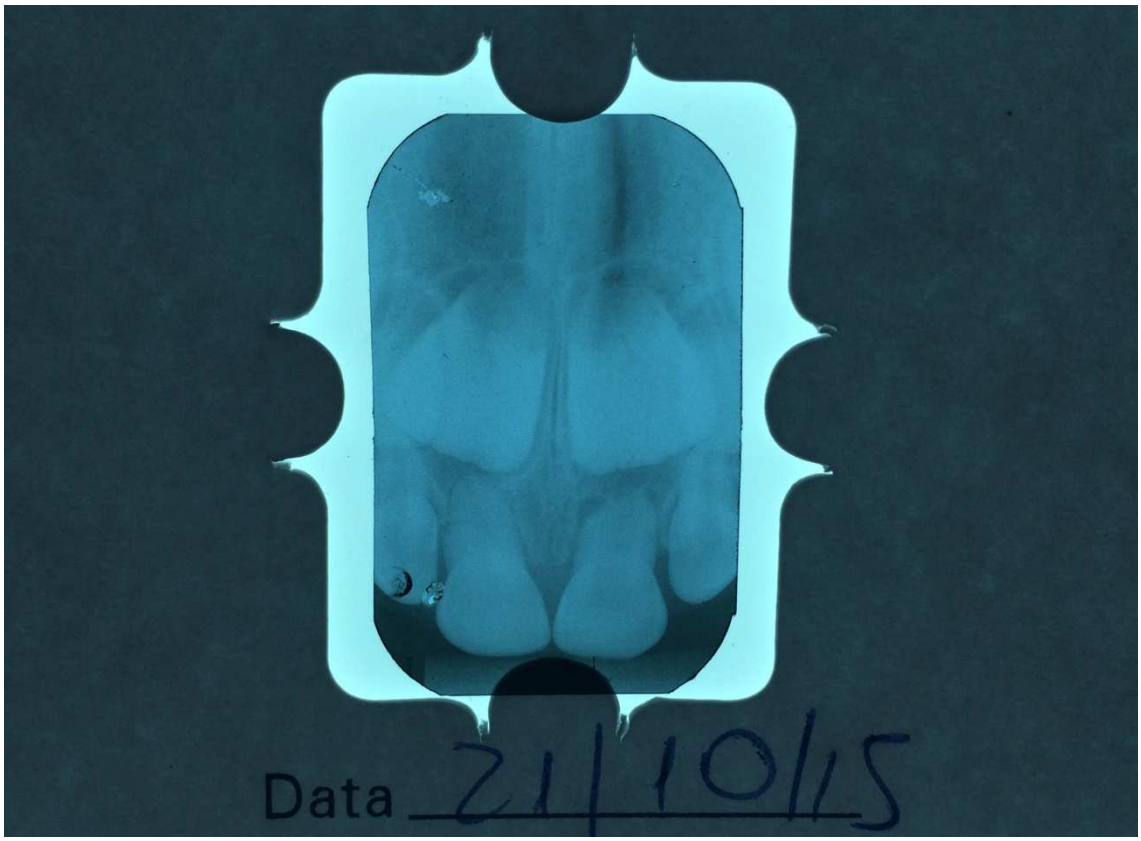
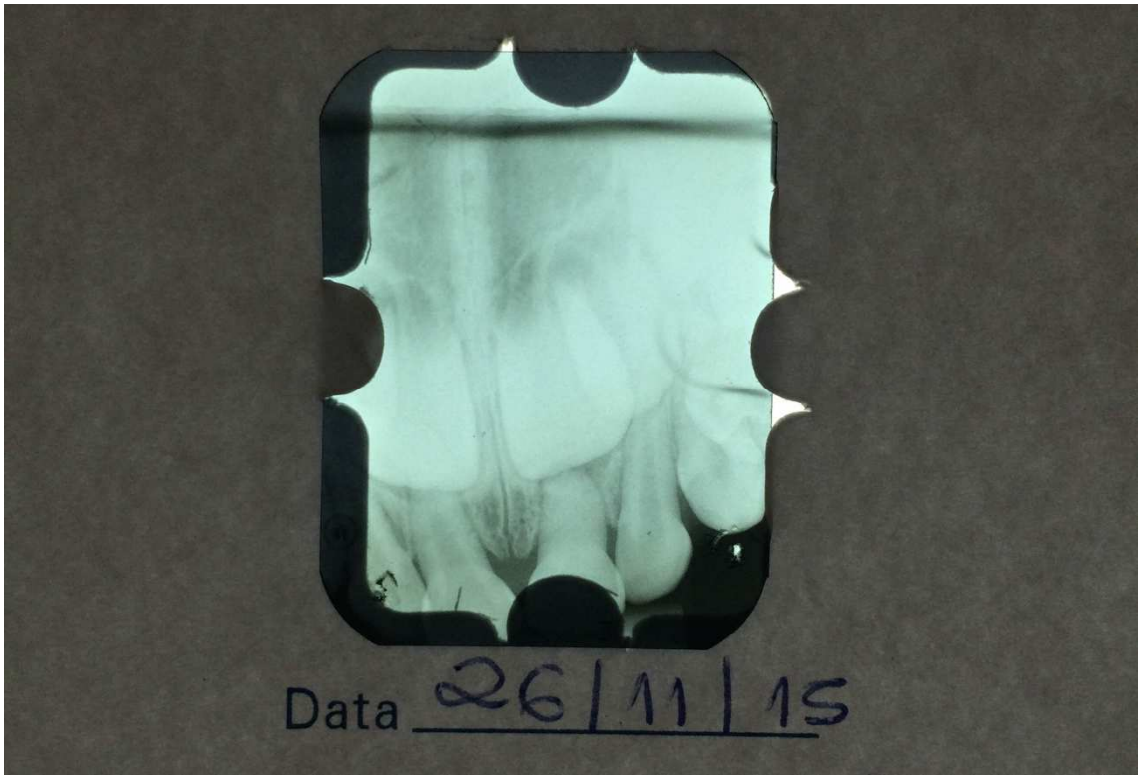
APPENDIX

APPENDIX A

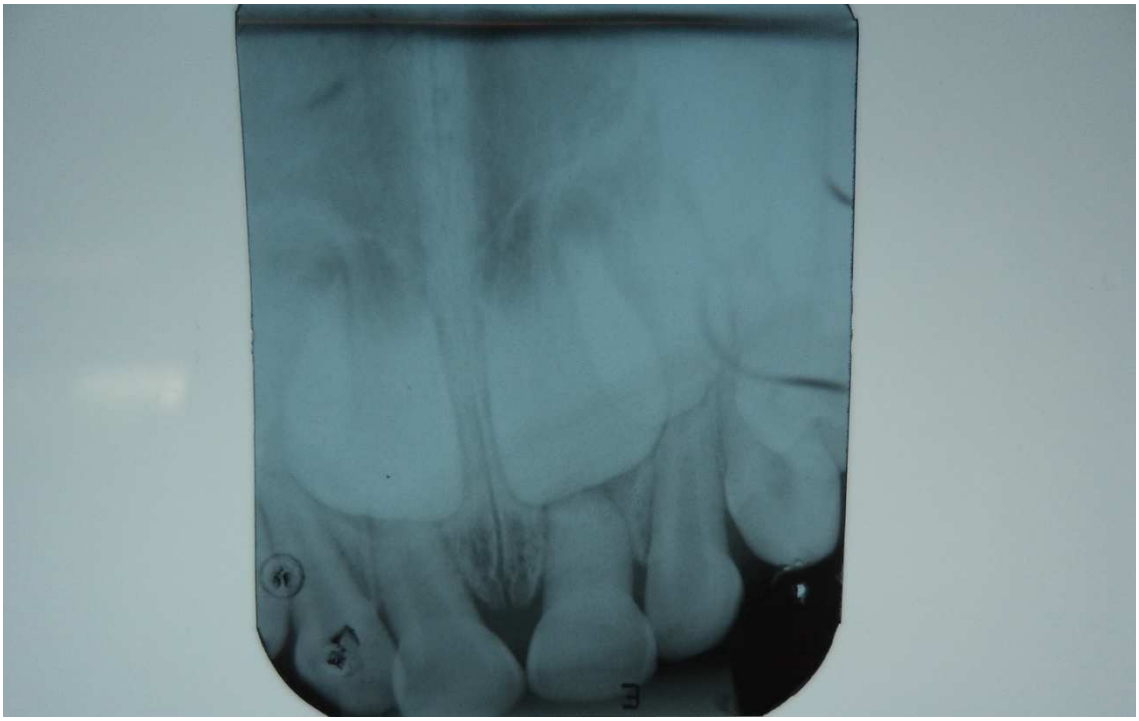
AJMR



APN



APN (melhor visualizar a obliteração)



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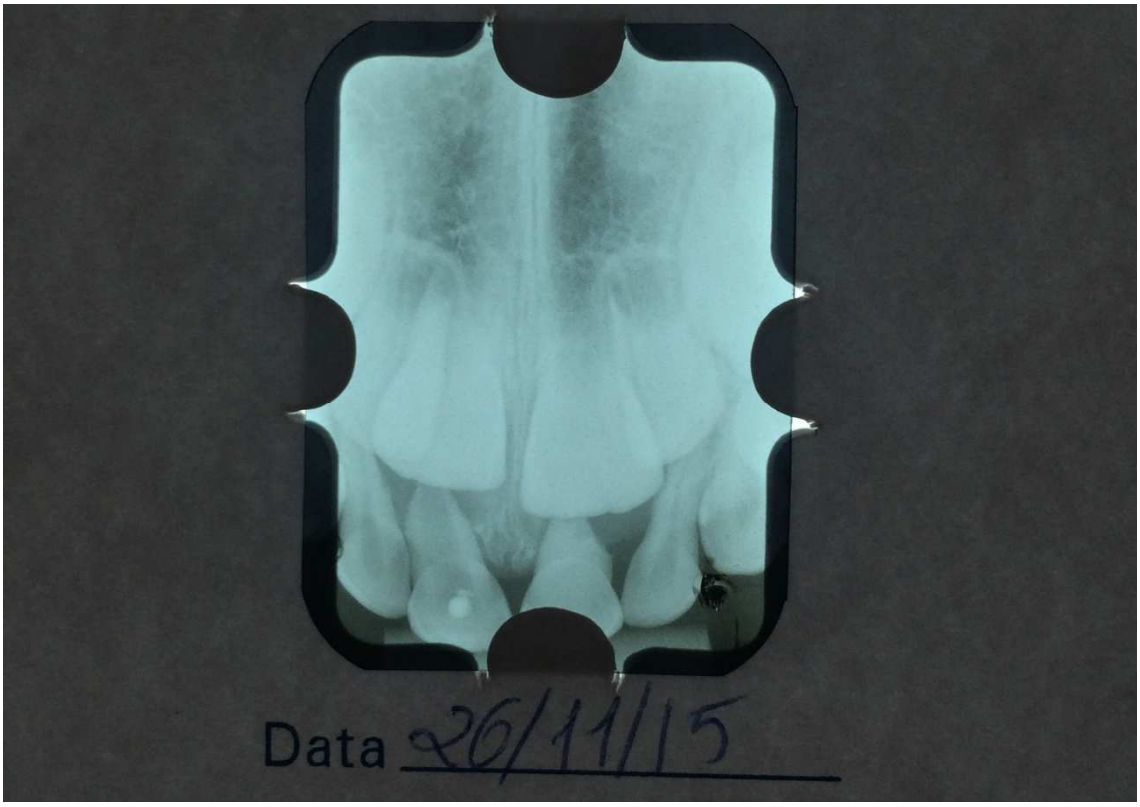
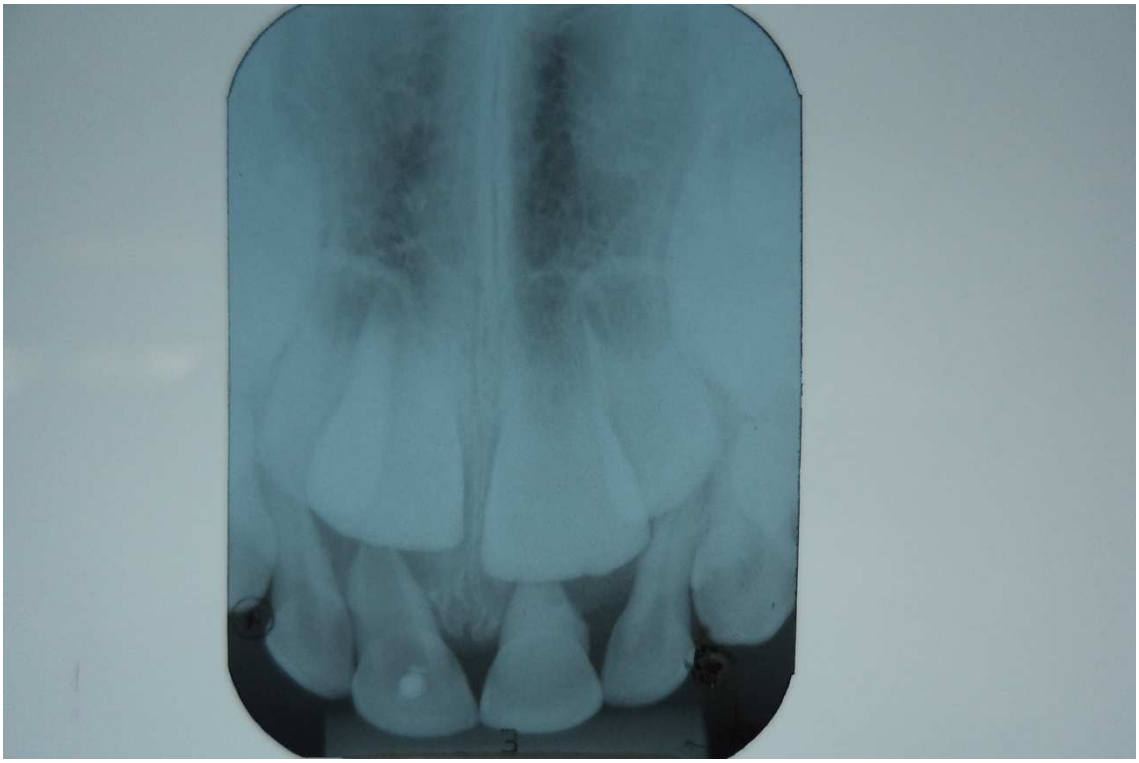


DHOP (melhor visualização da obliteração



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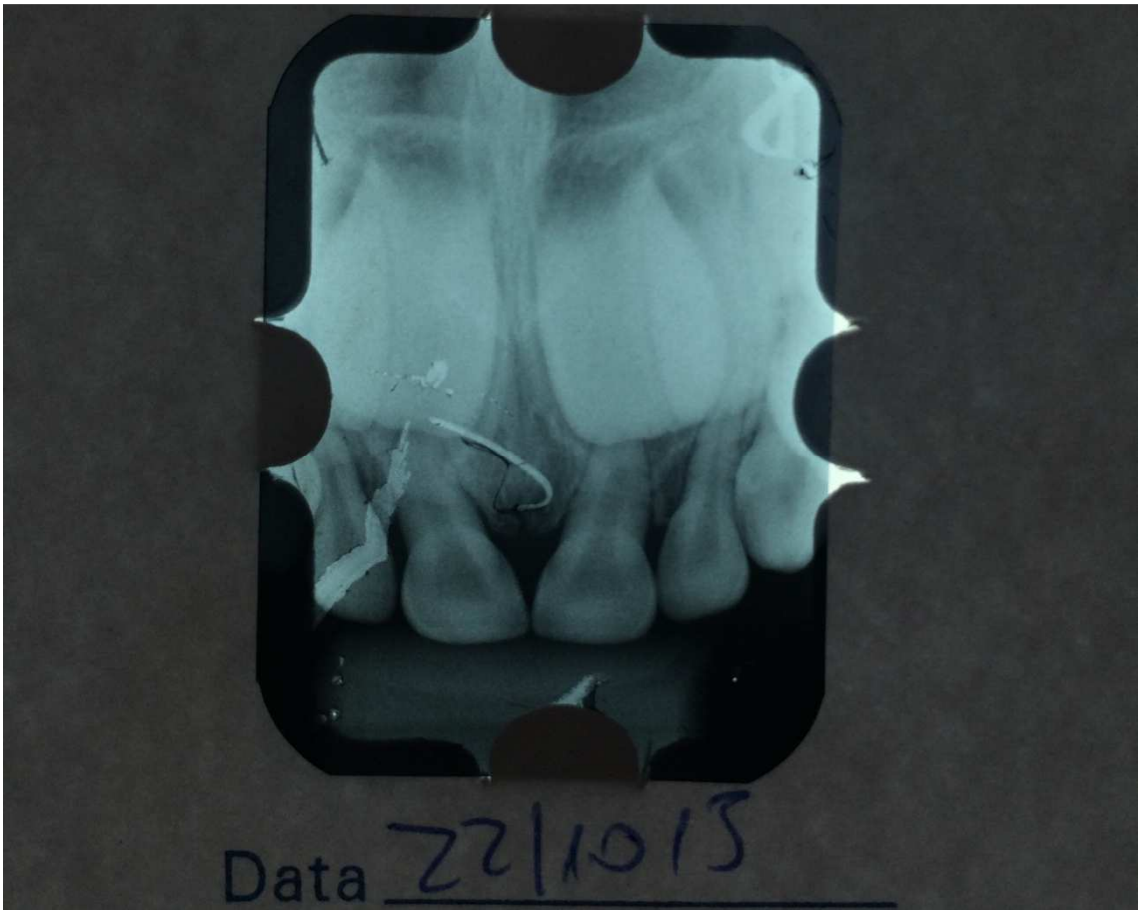

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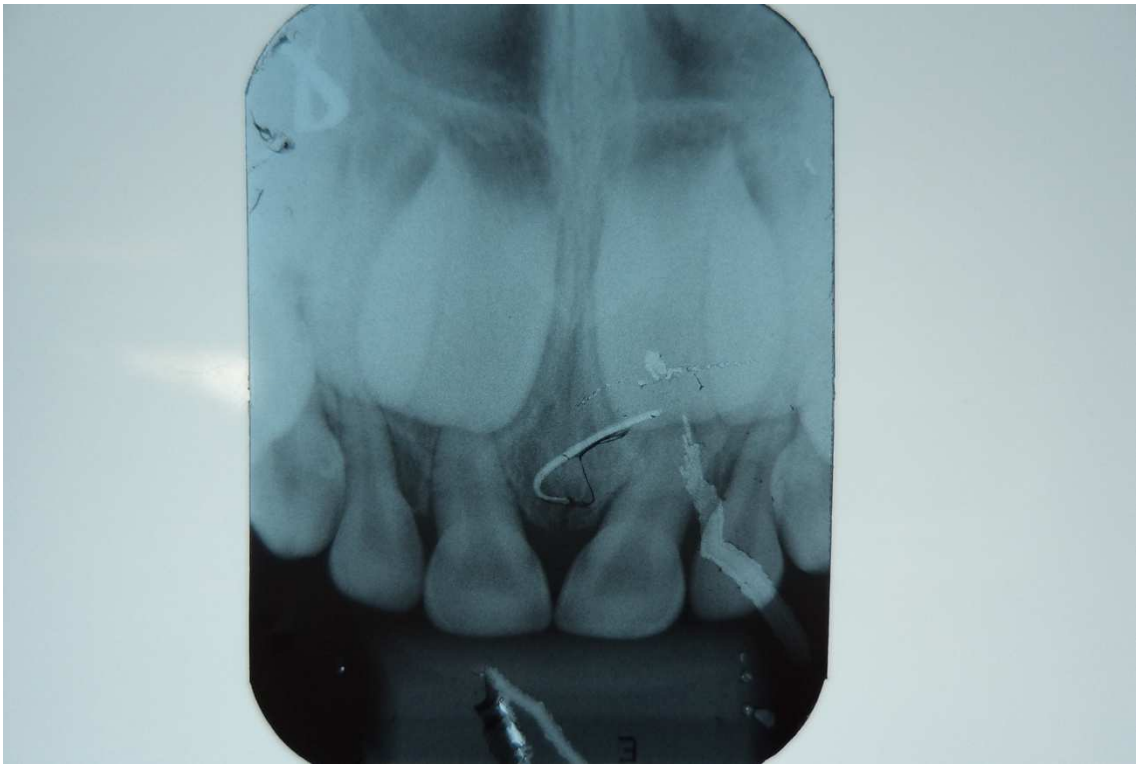

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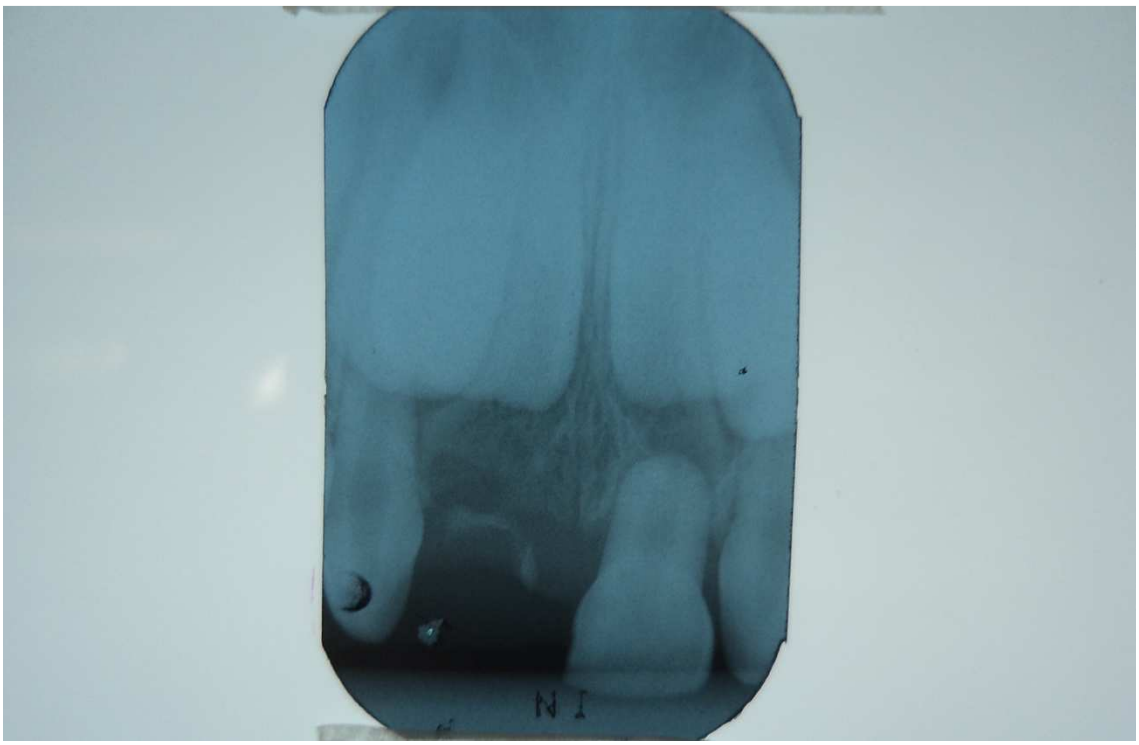

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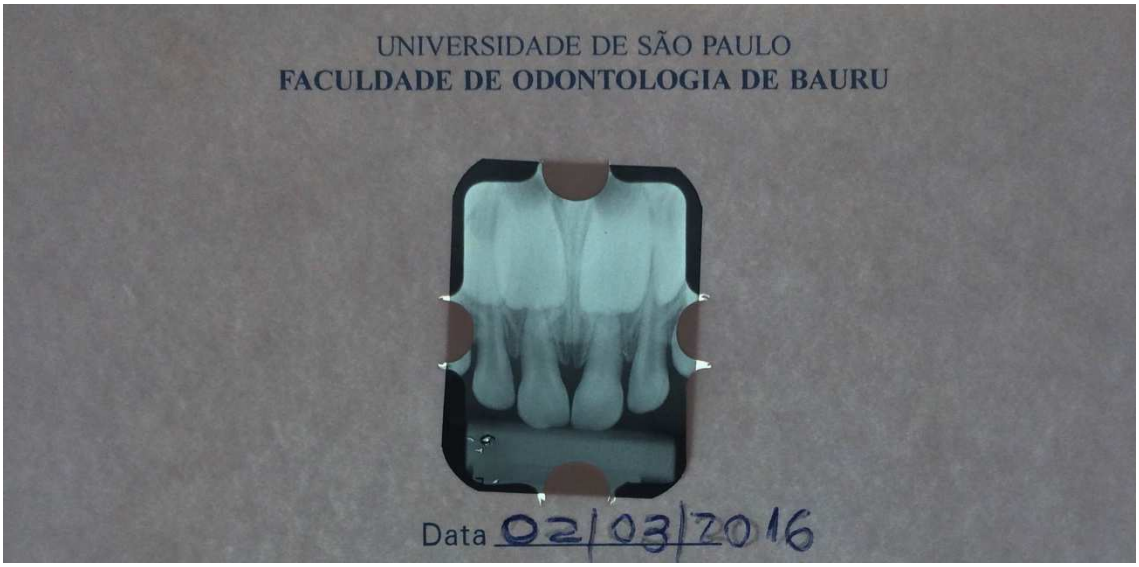
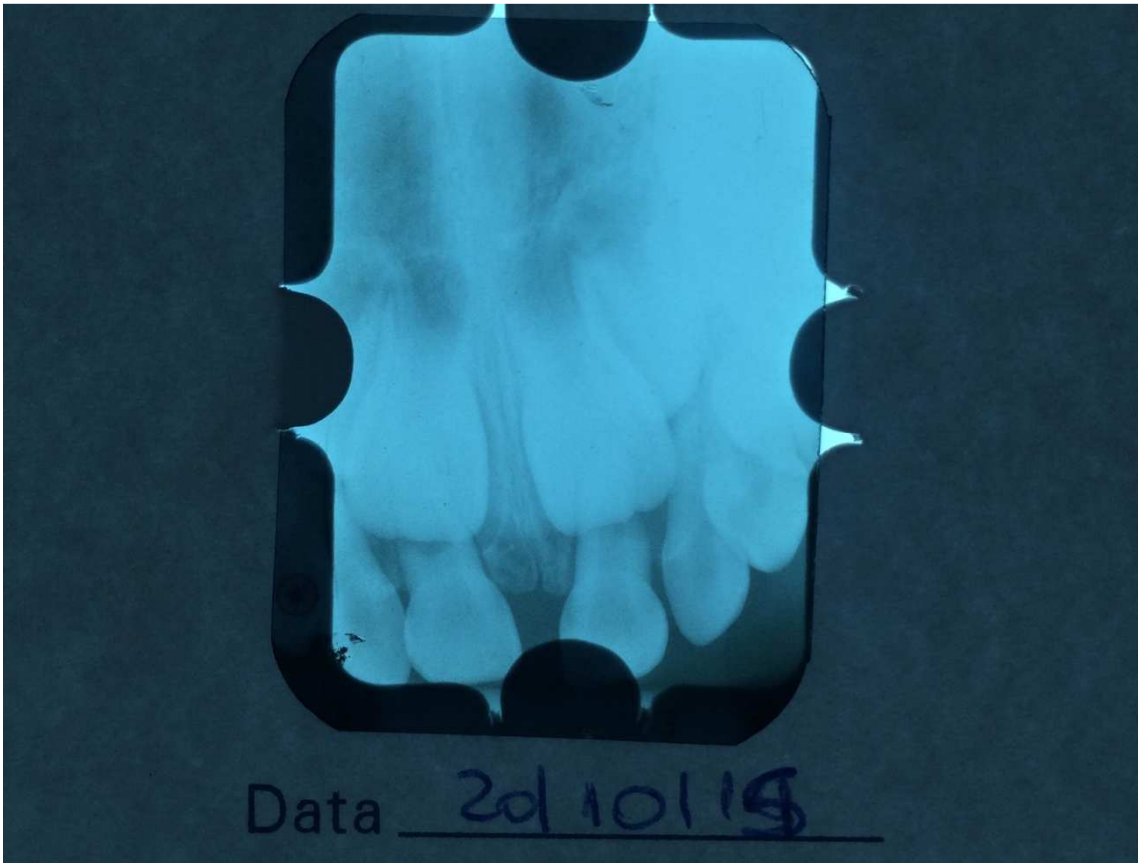

UNIVERSIDADE DE SÃO PAULO
FACULDADE DE ODONTOLOGIA DE BAURU
Data 02/03/2016

MVTM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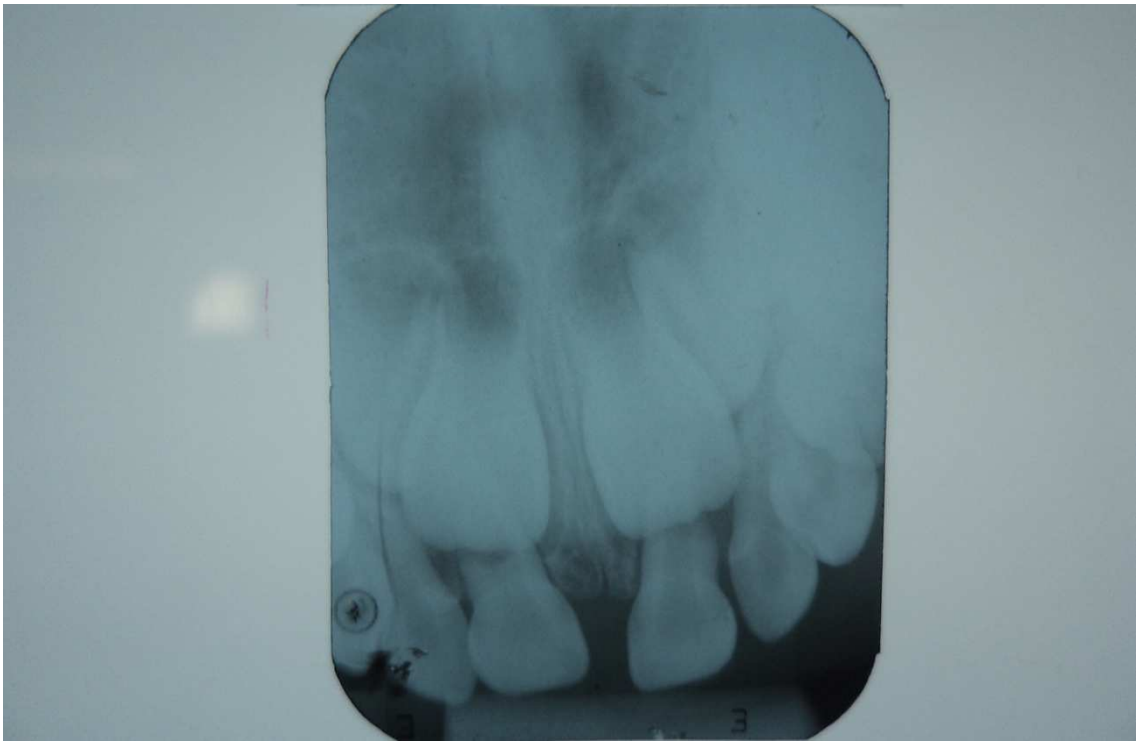

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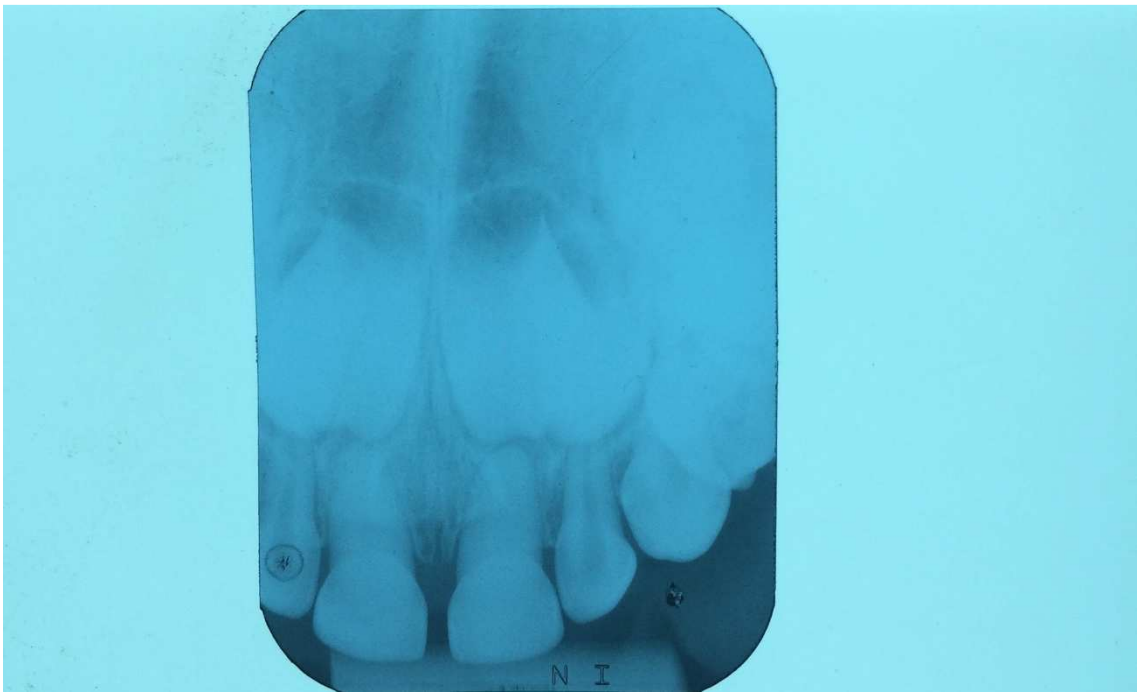

ANNEX

ANNEX 1

FACULDADE DE ODONTOLOGIA DE BAURU-USP

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Análise proteômica do fluido crevicular de dentes decíduos que sofreram traumatismo

Pesquisador: Maria Aparecida de Andrade Moreira Machado
Área Temática:
Versão: 2
CAAE: 48100115.9.0000.5417
Instituição Proponente: Universidade de Sao Paulo
Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.241.090

Apresentação do Projeto:
Idem ao parecer 1.198.759.

Objetivo da Pesquisa:
Idem ao parecer 1.198.759.

Avaliação dos Riscos e Benefícios:
Idem ao parecer 1.198.759.

Comentários e Considerações sobre a Pesquisa:
Idem ao parecer 1.198.759.

Considerações sobre os Termos de apresentação obrigatória:
Idem ao parecer 1.198.759.

Conclusões ou Pendências e Lista de Inadequações:
1- No projeto de pesquisa e TCLE informa que, "será coletada saliva de crianças entre 4 a 6 anos de idade"..., porém no projeto da Plataforma Brasil descreve que a coleta será realizada em crianças de 2 a 10 anos de idade, adequar estas informações.
PENDÊNCIA ATENDIDA. A pesquisadora informa que a faixa etária é somente para dentes decíduos e mudou o título da pesquisa, de 1 a 6 anos de idade.

Endereço: DOUTOR OCTAVIO PINHEIRO BRISOLLA 75 QUADRA 9
Bairro: VILA NOVA CIDADE UNIVERSITARIA **CEP:** 17.012-901
UF: SP **Município:** BAURU
Telefone: (14)3235-8356 **Fax:** (14)3235-8356 **E-mail:** cep@fob.usp.br

FACULDADE DE ODONTOLOGIA DE BAURU-USP

Continuação do Parecer: 1.241.090

2- Descreve que as crianças recrutadas serão as que estiverem matriculadas em escolas de educação infantil particular, municipais e estaduais, e também pacientes que estão em tratamento e/ou controle de rotina na clínica de Odontopediatria da Faculdade de Odontologia de Bauru – USP (FOB-USP). Por favor, informar qual será a forma de recrutamento. Se parte dos participantes da pesquisa forem recrutados nas escolas, deve-se incluir o termo de aquiescência de cada instituição.
PENDÊNCIA ATENDIDA. Foi anexado termo aquiescência da Secretaria Municipal de Educação o qual está o título do projeto maior que abriga o subprojeto em questão.

3- Com relação aos riscos inerentes a pesquisa descreve que os riscos são próximos de zero. Esta informação deve ser reformulada, já que os riscos que a pesquisa pode trazer são o desconforto e cansaço para a criança durante a coleta do material a ser utilizado na pesquisa.
PENDÊNCIA ATENDIDA.

4- No TCLE somente descreve que "Não haverá despesas decorrentes da participação do voluntário na pesquisa", esta informação poderia ser melhor descrita, detalhando que não haverá ressarcimento com alimentação e transporte, pois o participante da pesquisa pode entender que são os gastos relacionados com os material utilizados na pesquisa.
PENDÊNCIA ATENDIDA.

5- Reescrever o trecho do TCLE referente a entrega da via ao participante da pesquisa, substituir por "responsável pelo participante da pesquisa".
PENDÊNCIA ATENDIDA.

6- O item do protocolo de pesquisa na PB "Haverá retenção de amostras para armazenamento em banco?" Esta assinalado como "NÃO", entretanto sempre que houver coleta de material biológico em uma pesquisa, mesmo que o material seja descartado após seu processamento, esse campo da Plataforma Brasil deverá ser assinalado com a opção "SIM". Por favor, corrigir.
PENDÊNCIA ATENDIDA.

7- Arrumar o cronograma do projeto de pesquisa, o item coleta das amostras consta de julho a dezembro de 2015, entretanto as coletas devem ser realizadas somente aprovação do projeto de

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FACULDADE DE ODONTOLOGIA DE BAURU-USP

Continuação do Parecer: 1.241.090

pesquisa por este CEP. Atendida a pendência.

8- Com relação ao Termo de assentimento, como sugestão, poderia ser aplicado o Termo de assentimento somente para os participantes da pesquisa de 7 a 10 anos. Os participantes com idade inferior a 7 anos o pesquisador pode justificar que será aplicado um processo de assentimento (descrevendo como será realizado o processo. O processo de assentimento será de forma lúdica,etc.).
PENDÊNCIA ATENDIDA. Foi reformulado o TCLE para os responsáveis/pais dos participantes e o processo de assentimento.

Considerações Finais a critério do CEP:
Esse projeto foi considerado APROVADO na reunião ordinária do CEP de 16.09.2015, com base nas normas éticas da Resolução CNS 466/12. Ao término da pesquisa o CEP-FOB/USP exige a apresentação de relatório final. Os relatórios parciais deverão estar de acordo com o cronograma e/ou parecer emitido pelo CEP. Alterações na metodologia, título, inclusão ou exclusão de autores, cronograma e quaisquer outras mudanças que sejam significativas deverão ser previamente comunicadas a este CEP sob risco de não aprovação do relatório final. Quando da apresentação deste, deverão ser incluídos todos os TCLEs e/ou termos de doação assinados e rubricados, se pertinentes.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Folha de Rosto	folha de rosto 6.pdf	16/07/2015 19:50:34		Aceito
Outros	departamento de odp - 6.pdf	16/07/2015 19:59:18		Aceito
Outros	departamento de farmaco - 6.pdf	16/07/2015 19:59:41		Aceito
Outros	questionário final - 6.pdf	16/07/2015 20:00:05		Aceito
Outros	compromisso do pesquisador - 6.pdf	16/07/2015 20:00:35		Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TERMODECONSENTIMENTOLIVREEESCLARECIDO6Reformulado.doc	27/08/2015 22:41:13	Bella Luna Colombini Ishikiriama	Aceito
Projeto Detalhado	Projeto6Reformulado.docx	27/08/2015	Bella Luna	Aceito

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Continuação do Parecer: 1.241.090

/ Brochura Investigador	Projeto6Reformulado.docx	22:41:51	Colombini Ishikiriama	Aceito
Recurso Anexado pelo Pesquisador	RespostasCEPOdontopediatria.docx	27/08/2015 22:42:05	Bella Luna Colombini Ishikiriama	Aceito
Outros	TermodeaquiescenciaSecretariaMunicipaldeEducacao.pdf	27/08/2015 22:44:26	Bella Luna Colombini Ishikiriama	Aceito
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_552016.pdf	27/08/2015 22:46:16		Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

BAURU, 23 de Setembro de 2015

Assinado por:
Izabel Regina Fischer Rubira Bullen
(Coordenador)

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