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Oral Session O12 – Syndromes and Genetics 2

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Oral Session O12/Syndromes and Genetics 2

O12–84

Isolation and characterization of dental pulp stem cells from natal teeth

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Introduction: Dental pulp stem cells (DPSCs) were primarly derived from the pulp tissues of exfoliated deciduous teeth and permanent third molar teeth, while no report has yet been documented on deriving DPSCs from natal teeth. The aim of this study was isolation, identification and determination of the differentiation potential of putative mesenchymal stem cells (MSCs) derived from dental pulp of human natal teeth (hNDP).
Materials and methods: Ethical permission was obtained from Ethical Committee of Marmara University. The pulp tissues from two natal teeth of a newborn healthy female were digested using collagenase to generate single cell suspensions. hNDP-MSCs were analysed by flow cytometry, RT-PCR, Real Time-PCR, and immunocytochemistry. Furthermore, hNDP- MSCs were directionally differentiated towards adipogenic, osteogenic and chondrogenic lineages.
Results: In the flow cytometry analysis, hNDP-MSCs expressed CD10, CD13, CD44, CD90, CD166 and Oct-3/4, but not CD3, CD4, CD5, CD7, CD8, CD11b, CD14, CD15, CD19, CD34, CD45,CD117, HLA-DR, TRA-1-60, TR-1-80 and SSEA-4. Our immunohistochemistry (IHC) and RT-PCR findings indicated that hNDP-MSCs expressed some myogenic (desmin, myogenin, myosinIIa, and alfa SMA), neurogenic (gamma-enolase, MAP2a, b, c-fos, nestin, GFAP and betaIII tubulin), osteogenic (osteonectin, osteocalcin, osteopontin, and type I collagen) and chondrogenic (type II collagen) markers without stimulation towards differentiation in regular growth media. Real Time-PCR identified transcripts for embryonic stem cell genes Oct4, Rex-1, FoxD-3, Sox2, and Nanog. The differentiation potential of hNDP-MSCs to adipogenic, osteogenic and chondrogenic was shown by histochemical and IHC methods.
Conclusion: Stem cells derived from hNDP form a suitable source for tissue engineering and cell-mediated therapy.

O12–85

Mandibular phenotype in XLHED patients and Tabby model: CT and immunohistological analyses

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Introduction: X-linked Hypohidrotic Ectodermal Dysplasia (XLHED) is a rare disease characterized by developmental anomalies of ectodermally derived structures. The molecular etiology consists in a mutation in the *EDA* gene, coding for a morphogenetic factor called ectodysplasine-A1 (EDA-A1). The experimental model for XLHED is the mutant Tabby mouse. The dental phenotype in humans associates oligodontia of variable severity and morphological anomalies. Early implants therapy can be required in severe mandibular phenotypes and presents clinical challenges with high implants failure rates being described in children.
Materials and methods: CT (Computed-tomography) examinations were performed from 5 children affected by XLHED followed by 3D reconstructions with AMIRA (version 2.3) or SIMPLANT ™ softwares. Histological and immunohistological analyses were performed on sections of 10 Tabby and 10 Wild-type post-natal and adult mice mandibles and femurs demineralized in EDTA 15%. Masson Trichrome's staining was used to observe bone matrix and cellular components. Bone markers studied by immunofluorescence were osteopontin, osteonectin (SPARC), collagen I and Runx2, an osteogenic DNA-binding protein.
Results: CT mandibular sections showed mandibular hypoplasia, as well as hypercorticalization and increased local bone density in XLHED patients. Medullary bone hyperdensity in the symphyseal area was observed in mandibular 3D isosurface reconstructions. Massons trichrome's staining showed matrix bone heterogeneity in Tabby mouse, with reduced collagen staining and more cellular components. Immunofluorescence analyses revealed osteopontin and osteonectin stainings increase in the bone matrix of adult Tabby mice.
Conclusion: Mandibular hypoplasia and bone structural anomalies, potentially involved in implants failures, were observed in XLHED and require further analyses.

O12–86

Pre- and post-natal enamel formation of primary second molars in children with familial dysautonomia

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Introduction: Familial Dysautonomia (FD), also known as Riley–Day syndrome (MIM #223900) is an autosomal recessive disorder that affects children of Jewish Ashkenazi origin. It is classified as a hereditary sensory and autonomic neuropathy type III. FD affects the development and survival of sensory, sympathetic and parasympathetic neurons. It is present from birth, with a variety of symptoms, including gastrointestinal dysfunction, vomiting crises, recurrent pneumonias, altered sensitivity to pain and temperature, and cardiovascular instability. The second primary molar begins the calcification around 20 weeks *in utero* and crown is completed at 1 year. The aim of this study was to evaluate the pre- and postnatal effects of FD on the development of enamel in maxillary second primary molars.
Materials and methods: Seven FD maxillary primary second molars were compared to 13 normal teeth. BL slices connecting the mesial cusps were prepared from each tooth and the total thickness and ratio of pre/total enamel was measured.

Results: FD teeth showed reduced BL dimensions at the CEJ. Total enamel width was similar in both groups. Prenatal enamel thickness in FD was larger and the ratio to total enamel thickness was greater. The most significant feature observed in FD primary molars was the great number of post-natal traumatic lines in the enamel, probably attributed to traumatic events during the first year of life in these children.
Conclusion: FD primary molars showed thicker pre-natal enamel formation and significant increased number of post-natal traumatic events compared to controls.

O12–87

Mutations of the SH3BP2 gene in two families with Cherubism

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Introduction: Cherubism is a rare autosomal dominant syndrome characterized by abnormal bone tissue in the lower part of the face. Both mandible and maxilla are enlarged and replacement with large amounts of fibrous tissue occurs, which cause a characteristic facial swelling with painless and cyst-like growth. Mutations in the gene coding for SH3BP2 have been identified in about 80% of people with cherubism. In most of the remaining cases, the genetic cause of the condition is still unknown.
Materials and methods: Two cases of the aggressive form of Cherubism were described in two Turkish families with extremely extensive swelling in the bilateral mandible, typical pathological features and familial history. The study was approved by the institutional review boards and written consent was obtained from the parents. Genomic DNA was extracted from individuals of two families and mutation in the SH3BP2 gene was detected by PCR and direct DNA sequencing was carried out.
Results: In the first family, a missense mutation Arg415Gln was found in exon 9 of the SH3BP2 gene in all affected individuals. The unaffected individuals did not have this mutation. In the second family, another missense mutation Pro418Thr was identified in exon 9 of the SH3BP2 gene in patient and his mother with cherubism. His father without cherubism did not carry the mutation.
Conclusion: We detected the point mutations in the SH3BP2 gene in our patients with multiple affected individuals and demonstrated that genetic analysis is a useful method in the identification of cherubism.

O12–88

Oral health in 22q11-deletion syndrome; parental perspectives in a grounded theory study

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Introduction: 22q11-deletion syndrome (22q11DS) is one of the most common multiple anomaly syndromes with an incidence around one per 4000 newborns. As diagnostic methods are relatively new the syndrome is under diagnosed. Oral health issues have just recently been addressed and include e.g., mineralization disturbances, caries problems and hyposalivation. The aim of this study was to explore and describe parents' assessments and considerations of orofacial problems and treatment needs in their children with 22q11DS.
Materials and methods: In-depth interviews focusing on oral health were carried out with 12 parents. Interviews were transcribed verbatim and analysed according to grounded theory.
Results: A core category was identified and named 'fighting against all odds in order to gain a good oral status in their child', and included perceptions of how the diagnosis had implied legitimacy to the child's oral health problems. Parents described dental problems like severe decay, or defect enamel leading to discoloured teeth. Problems not always understood by the dental teams. Receiving a medical diagnosis was important and the parents described a transition from dentists blaming the parents for their children's dental problems to understanding what it was all about. This study shows that parents perceive that dental health professionals don't fully understand the impact of medical issues on oral health until a defined medical diagnosis is established. Conclusions: In the eyes of parents, a defined medical diagnosis is important to gain legitimacy for oral health problems in the encounters with dental health professionals.

O12–89

The genetic basis of a dentigerous cyst associated with a supernumerary tooth?

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Introduction: Supernumerary teeth are teeth additional to the normal complement and the frequent clinical indicators are non-eruption or delayed eruption of teeth, crowding, displacement and dentigerous cyst (DC) formation. Approximately, 95% of DCs involve the permanent dentition and only 5% are associated with supernumerary teeth. The objectives of this study were to: (i) report a pair of siblings with supernumeraries of whom, one developed a dentigerous cyst and (ii) analyze fragile histidine triad (FHIT) and p53 gene status in DC associated with supernumerary teeth.
Clinical Management: This six-year-old Chinese boy complained of swelling in the maxillary right incisor region. Radiographs revealed the presence of two supernumeraries in the premaxillary region, one of which had evidence of an enlarged follicle. Histopathology confirmed that the cystic lining was consistent with a DC. The patients elder sister also exhibited two supernumeraries in the premaxilla which was subsequently surgically removed. Blood samples were collected and the DNA extracted using the Qiagen® mini blood kit. The DNA yield was quantified using 260 nm/280 nm ratio. After isolation, aliquots of the DNA samples were prepared for analyzing the status of the FHIT and p53 gene.
Conclusion: Occurrence of supernumerary teeth in siblings indicates that inheritance is a major contributory factor in their development. Although DCs are uncommon in the first decade of life, regular inspections of radiographs are important. It is hypothesized that aberrations of FHIT and p53 genes could be considered as markers responsible for the development of DCs associated with supernumerary teeth.

O12–90

Truncations of PAX9 and nonsyndromic oligodontia – an Indian perspective

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Introduction: Development of dentition has multiple genetic regulators and minute disturbances in the blueprint leads to severe

phenotypes like Oligodontia and Hypodontia. The role of PAX9 as an important transcription factor regulating the agenesis of teeth has been documented on an individual case basis. The familial occurrence of oligodontia is an extremely rare finding with only fifteen sporadic cases reported worldwide indicating the association of PAX9 with teeth agenesis.

Clinical Management: The present molecular study from India involves probands over two generations (mother and three children) exhibiting non-syndromic Oligodontia. Clinical and Radiological evaluation details of missing teeth in probands were used to describe the occurrence of Oligodontia coupled to truncation of important exons of PAX9. In the probands the missense mutations in exon 2 and deletions in exon 1 and 4 are probably leading to the manifestation of these phenotypes. The mutations are particularly interesting as they are located outside the critical 'paired domain' in exon 2. The substitution and missense study reveals the critical genetic role of this important DNA binding protein in developing a nonsyndromic oligodontia.

Conclusion: This is the first reported case from Indian subcontinent and these findings can be utilized as important early diagnostic tools for detection and forecasting appropriate management of the dental abnormalities in children.

O12–91

New mutation of *PAX9* gene in a patient with hypodontia

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Introduction: The morphogenesis of teeth is under strict genetic control. The most important events during the regulation of tooth development are inductive interactions between the epithelial and mesenchymal tissues. The expression of Pax9 has been shown to specifically mark the mesenchymal regions at the prospective sites of all teeth prior to any morphological manifestations. For this reason, we choose PAX9 gene as a candidate gene to seek the pathological mechanism of hypodontia.

Patients and methods: All study protocols were approved by the Ethical Committee of Peking University Health Science Center (approval number: IRB00001052-06072). Nineteen unrelated Chinese patients with clinical diagnosis of hypodontia were included in this study. Among them, fourteen patients were familial cases and the rest were sporadic cases. Informed consent was obtained from the patients or their parents. Mutation analysis (PCR, direct sequencing and restriction enzyme analysis) was used in this study.

Results: Mutation analysis revealed a novel heterozygous c.480C > G mutation in one patient who misses 20 permanent teeth (the third molars excluded) and 6 primary teeth.

Conclusion: A premature stop codon was induced in exon2, and the mutation may undergo nonsense-mediated mRNA decay (NMD) process. In the NMD pathway, abnormal mRNA whose stop codons appear in the coding region except for the last coding exon will be recognized and removed. The severe phenotype may result from haploinsufficiency of PAX9. This work was supported by Beijing Municipal Natural Science Foundation No. 7022022 and No.7092112.

