Investigation of genes and gene proteins in cleft affected tissue

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Objectives. Craniofacial cleft morphopathogenesis is relatively unclear. It has been associated with cleft candidate genes which encode proteins that regulate facial tissue formation and differentiation but the distribution of these proteins in cleft affected tissue and interactions between them have not been well documented. The main aim of this study was to evaluate and compare the presence of cleft candidate gene coded protein containing cells within different cleft tissue types.

Materials and methods. Cleft tissue was arranged into 3 groups – unilateral cleft lip (UCL) with 36 patients, bilateral cleft lip (BCL) with 13 patients, cleft palate tissue (CP) with 26 patients. Oral mucosa tissue was obtained during cleft correcting surgery. Control groups were formed from patients without clefts (7 patients who had upper lip frenulum plastic surgery and 5 patients from the historical collection of the Institute of Anatomy and Anthropology of Rīga Stradiņš University). Immunohistochemistry was implemented to detect BarH-like Homeobox 1 (BARX1), Distal-less Homeobox 4 (DLX4), Forkhead Box E1 (FOXE1), Homeobox B3 (HOXB3), Muscle Segment Homeobox 2 (MSX2), Paired Box Transcription Factor 7 (PAX7) and 9 (PAX9), Receptor-like Tyrosine Kinase (RYK), Sonic Hedgehog (SHH), SRY-box Transcription Factor 3 (SOX3), Wingless-type MMTV Integration Site Protein 3A (WNT3A) and 9B (WNT9B) positive cells.

Results. Cleft candidate gene protein containing cells were detected in all patient and control groups with different distributions. Multiple statistically notable correlations were found between the evaluated proteins.

Conclusions. Healthy oral cavity tissue is characterized by WNT9B, WNT3A, and SOX3 being the most prominent, in moderate number – SHH, PAX7, HOXB3, FOXE1, practically no presence of BARX1 and MSX2 containing cells. UCL is characterized by the increase of BARX1, FOXE1, HOXB3 and PAX7; BCL – by the increase in DLX4, PAX9, and a decrease in SHH. All cleft phenotypes, including CP, had increased MSX2 and RYK and decreased SOX3, WNT3A, WNT9B in tissue.