ImmunoTools *special* Award 2015

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Abnormal craniofacial development and tissue repair

Many birth defects are associated with craniofacial malformations. Cleft lip and palate (CLP) is one of the most frequently occurring congenital craniofacial anomalies. Our department Orthodontics and Craniofacial Biology (Dentistry) aims to ameliorate the complex treatment of craniofacial patients. The presence of the largest CLP centre of the Netherlands fuels both clinical and preclinical research in this area. The children are treated by a multidisciplinary cleft team, however, despite surgical closure of the cleft, excessive scar formation may further contribute to the morbidity. The scarring impairs growth and development of the upper jaw and the dentition, and interferes with muscle regeneration in the soft palate.

Palatogenesis is a complex process in which the palate is formed from the two opposing palatal shelves. First they elevate and grow towards each other, next adherence of the epithelial fronts takes place and finally this epithelial barrier layer disappears allowing the fused mesenchym to form the bony hard palate and the muscular soft palate. The formed palate then separates the oral from the nasal cavity allowing speech, eating, and swallowing. Unfortunately, cleft patients often keep having difficulties with eating, speaking, swallowing, and hearing.

Cranial neural crest cells (CNCCs) are multipotent stem cells that migrate from the dorsal neural tube into the frontonasal area where they are pivotal for the formation of various cell types, including bone, cartilage, neurons, and smooth muscle. Defects in the generation, proliferation, migration and differentiation of these CNCCs are likely important determining factors for craniofacial abnormalities. Although both genetic and environmental factors are important for the etiology of CLP it is still unclear which molecular and cellular mechanisms are responsible for clefting.

We are investigating the different signaling pathways that determine these different processes. These signaling pathways include cytokine-cytokine receptor signaling, adhesion molecule signaling, transcriptional signaling, and Wnt, Sonic hedgehog, Mapkinase, and Akt signaling.

These inter- and intracellular signaling pathways determine whether cells express the correct proteins in the right amount and within the correct timeframe, and whether the necessary developmental and regenerative processes can occur.

In our laboratory, we study both the molecular mechanisms and the cellular events that are involved in scar formation and that trigger cleft formation. In addition, we target cytoprotective mechanisms that may rescue or prevent cleft and/or scar formation. Hereto we make not only use of various *in vitro* and *in vivo* wound repair models, but also of a wealth of developmental models in mice, zebrafish, and organ/cell culture systems. A better understanding of the protective mechanisms in relation to these anomalies may lead to novel preventive and therapeutic opportunities.

Antibodies, chemokines and cytokines from ImmunoTools would help us tremendously in deciphering how the palate is formed, and how cell migration, differentiation, proliferation, and apoptosis determine the difference between normal palatogenesis and cleft formation. Moreover, this would facilitate elucidating the decisive signaling pathways that are involved in the epithelial-mesenchymal cross-talk that drives both palatogenesis and tissue repair.

I expect that our combined clinical and laboratory research will increase the understanding of the etiology and prevention of CLP and scar formation following surgery. We are convinced that this will ultimately result in better treatment modalities.

ImmunoTools *special* AWARD for **Frank Wagener** includes 25 reagents

FITC - conjugated anti-human CD11b, CD54, CD62E, CD62P, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

recombinant human cytokines: rh IL-37, rh I-TAC / CXCL11, rh PF4 / CXCL4,

rh PF4v1/CXCL4V1, rh TGF-beta3

FITC - conjugated anti-mouse CD11b, CD54, Gr-1, NK-cells, isotype control IgG2b

recombinant mouse cytokines: rm CXCL9, rm IP-10 / CXCL10, rm PF-4, rm SDF-1a / CXCL12a, rm SDF-1b / CXCL12b, rm TNFa, rm VEGF

DETAILS more AWARDS