

SERIAL ANALYSIS OF GENE EXPRESSION DURING MOUSE TEETH DEVELOPMENT AT DAY E 14.5 THROUGH THE EUREXPRESS INITIATIVE

[A. Bloch-Zupan](#)^{1,2,3,4}, A. Marx², M. Hamou², R. Huli², [P. Dollé](#)¹

¹ [IGBMC](#) (*Institut de Génétique et de Biologie Moléculaire et Cellulaire*), Department of Physiological Genetics, Inserm, U596, CNRS, UMR7104, Illkirch, FR

² [Faculty of Dentistry](#), Louis Pasteur University, 1 place de l'Hôpital F-67000 Strasbourg Cedex FR

³ Reference Centre for Dental Manifestations of Rare Diseases, Service de Soins Bucco-Dentaires, Centre Hospitalier Universitaire, Strasbourg, FR

⁴ [Eastman Dental Institute](#), [Institute of Child Health](#), London UCL, UK

INTRODUCTION: Odontogenesis is under strict genetic control. Genes that regulate tooth development are being identified with increasing speed. More than 300 genes are included in the graphical database illustrating the gene expression patterns during tooth development (<http://bite-it.helsinki.fi>). Ascertaining when and where genes are expressed is of crucial importance in order to understand the physiological role of a given gene/protein and the interactions between them. In addition, the normal expression patterns can then be compared to those observed in a variety of pathological conditions to identify pathological hallmarks of gene expression. This has helped understanding how the corresponding genes regulate tooth formation, and how aberrant functions of specific genes cause dental defects.

METHODS: To accelerate the discovery of new genes involved in tooth development we have undertaken a systematic approach using the EURExpress database detailing expression patterns of genes during mouse teeth (molars and incisors) development at the cap stage (E14.5). This stage is characterised by histomorphogenesis of the enamel organ, formation of signalling centres (the primary enamel knots) and condensation of the underlying ectomesenchyme. It is potentially a critical stage regarding anomalies of teeth number, size, shape and structure with the individualisation of the inner dental epithelium from which ameloblasts originate. EURExpress (<http://www.eurexpress.org>) an integrated project funded by the EU under the 6th Framework Program, is implementing a transcriptome-wide atlas of gene expression patterns by means of in situ hybridisation (ISH) with non-radioactive probes, which is implemented in real time in a freely accessible web-linked database. The final goal of the project is to analyse expression data of > 20,000 genes by RNA in situ hybridisation on serial sagittal sections from E14.5 wild type C57B16 murine embryos. These data will result in a detailed description (at a cellular level) of gene expression patterns in the developing mouse. The “transcriptome atlas” is generated using a newly developed automated RNA in situ hybridisation system.

RESULTS: We created a database for “Odontogenesis”, allowing automatic recollection of expression patterns within tissues of interest whether epithelial or mesenchymal. Are considered localisation, intensity and homogeneity of ISH signals. A differential comparison is made with other neighbouring regions of the embryo. An ubiquitous distribution of transcripts or absence of signals are also recorded. Selected images are integrated in the database allowing a quick identification of the expression patterns within incisor and molar tissues. Today more than 400 genes have been analysed. Eventually the database will include the expression data of all the mouse genes analysed through EURExpress.

DISCUSSION & CONCLUSIONS: Data will be scrutinised to discover new genes involved in tooth development, and pinpoint signalling pathways and synexpressions groups. We will also compare the teeth expression data with eye and ear expression data analysed by other members of the research group using similar approaches. This comparative approach is similar to a syndromic phenotyping approach gathering data from different systems and organs to facilitate diagnosis of syndromes combining teeth, eye and ear features.

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