IDGenes: A reference database for dynamic modelling of genetic interactions in the developing mouse brain

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The emergence of the neural tube from the neural plate and the patterning of these structures along their anterior-posterior, dorsal-ventral and medial-lateral axes are fundamental processes during vertebrate neural development. These processes are determined by well defined and locally restricted expression of genes and their gene regulatory networks.

Here we present the *IDGenes* database, which functions as a reference database for the genetic interactions in the developing mouse brain. It can be found at www.helmholtz-muenchen.de/idgenes. So far the database offers detailed information about the expression of genes and their genetic interactions in the developing mid-/hindbrain region. This database is conceived for a continuous expansion of stored gene expression and interaction data by allowing new data input from users. The information stored in *IDGenes* can be used for dynamic modelling of regulatory mechanisms under the consideration of spatial and temporal extensions in the mouse brain (see Wittmann et al. 2009 [1]). Currently, 86 gene expression datasets and 156 genetic interaction datasets assigned to different anatomical regions at the stages E8.5, E10.5 and E12.5 of mouse embryonic development (see Figure 1) are available from the database.

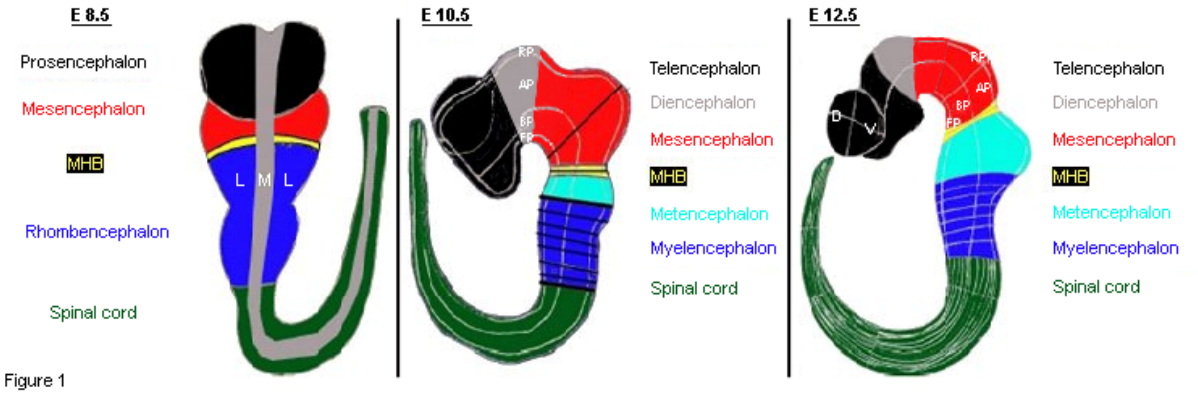

Figure 1

The discovery of new gene regulatory networks interaction partners, in particular of signalling cascades and transcription factors regulating the expression of key genes involved in neural plate/tube development, is currently of great interest [2]. In this context, the Wnt signalling pathway plays a crucial role because of its participation in the regulation of regional patterning, cell cycle, cell fate specification, cell differentiation, cell survival but also because

of its involvement in various human diseases. Tcf/Lef transcription factors are the downstream nuclear effectors of the canonical Wnt signalling pathway, and their interactions with putative Wnt target genes have been predicted using a Support Vector Machine (SVM). Target genes of the Wnt pathway known to be directly activated by Tcf/Lef factors or indirectly activated by other factors are derived from the *IDGenes* database. Subsequently, in-silico promoter analysis of these target genes has been performed and the number of evolutionary conserved Tcf/Lef transcription factor binding sites as well as the matrix similarities have been used as training dataset. By applying test data to the statistical model computed from the SVM the genes Lef1 and Dkk3 are predicted to be directly activated by the Wnt signal. qPCR analyses of mice overexpressing Wnt1 in the adult brain in fact strongly suggest Lef1 as a direct target gene of the Wnt signalling pathway.

References:

[1] Wittmann DM, Blöchl F, Trümbach D, Wurst W, Prakash N, et al. (2009) "**Spatial Analysis of Expression Patterns Predicts Genetic Interactions at the Mid-Hindbrain Boundary"** *PLoSComput Biol* **5(11)**: e1000569.

[2] Prakash N, Puelles E, Freude K, Trümbach D, Omodei D, Di Salvio M, Sussel L, Ericson J, Sander M, Simeone A, Wurst W. (2009) "**Nkx6-1 controls the identity and fate of red nucleus and oculomotor neurons in the mouse midbrain"** *Development* **136(15)**: 2545-2555