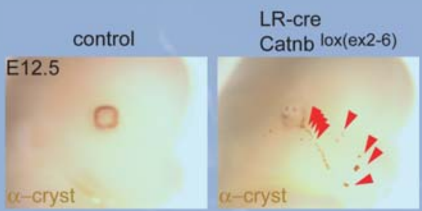
Zbyněk Kozmik

kozmik@img.cas.cz

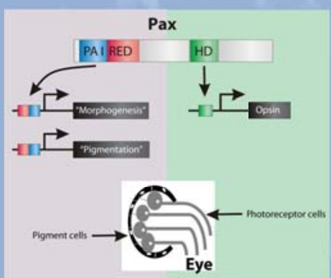
Laboratory of Transcriptional Regulation

Eye development and evolution, Pax genes

Zbyněk Kozmik, PhD / Head of Laboratory
Ondřej Machoň, PhD / Research Scientist
Tomáš Vacík, PhD / Research Scientist
Jitka Láchová, MSc / Research Assistant
Veronika Nosková / Technician
Iryna Kozmiková, MSc / PhD Student
Jana Růžičková, MSc / PhD Student
Naoko Fujimura, MSc / PhD Student
Lubica Škultétyová, MSc / PhD Student
Pavel Vopálenský, MSc / PhD Student
Kristýna Jonášová / Diploma Student
Veronika Gabanová / Diploma Student
Barbora Antošová / Diploma Student
Daniela Gurská / Diploma Student



Ectopic lens formation in the absence of β-catenin gene function (Kreslova et al., 2007)



The´Paxcentric´ (bipartite, PD-HD) model proposes an evolutionarily conserved function for paired domain in pigmentation (and morphogenesis) and for homeodomain in opsin gene regulation, respectively. The fascinating feature of the proposed model is that the morphological unity found in the eye, a photoreceptor linked to the shading pigment, is mirrored at the molecular level, by uniting two independent DNA-binding domains in one regulatory protein: Pax.

Research topics

We are interested in the genetic basis of mammalian eye and CNS development. Our focus is on the role of transcription factors and signalling cascades, especially on the role of *Pax* genes and Wnt/β-catenin pathway. A combination of gain-of-function (transgenic) and loss-of-function (conditional knock-outs) approaches are used.

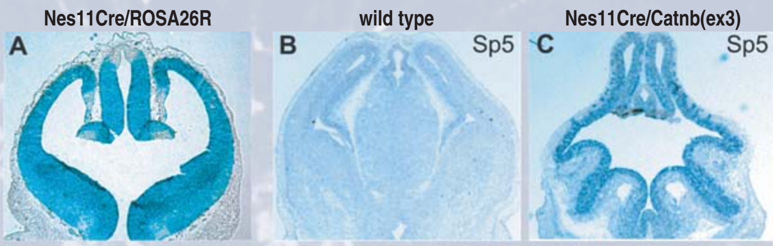
Our second main interest is eye evolution. Several model systems including mouse, amphioxus, scallop, medaka and jellyfish are used in the laboratory. Early morphological studies have suggested that eye has evolved multiple times during the course of evolution. In contrast, more recent genetic data indicate a central role of Pax6 in eye development in most animals. We have recently proposed a model that two independent DNA-binding domains within a single Pax transcription factor have been co-opted for two essential features of the proto-eye: production of a dark pigment and production of a photopigment. Experiments are under way to test this bipartite model. In addition, we are looking at the role of other genes acting dowstream of *Pax* in the regulatory cascade (e.g. *Six, Eya* or *Dach* genes), which are highly evolutionarily conserved.

Current grant support

AS CR (AV0Z50520514), Ministry of Education, Youths and Sports (Center for Applied Genomics 1M0520), GA AS CR (IAA500520604)

Selected recent papers

1. Kozmik Z, Holland ND, Kreslova J, Oliveri D, Schubert M, Jonasova K, Holland LZ, Pestarino M, Benes V, Candiani S. Pax-Six-Eya-Dach network during amphioxus development: conservation in vitro but context specificity in vivo. **Dev Biol.** 2007;306:143-59.
2. Kreslova J, Machon O, Ruzickova J, Lachova J, Wawrousek EF, Kemler R, Krauss S, Piatigorsky J, Kozmik Z. Abnormal lens morphogenesis and ectopic lens formation in the absence of beta-catenin function. **Genesis.** 2007;45:157-68.
3. Fujimura N, Vacik T, Machon O, Vlcek C, Scalabrin S, Speth M, Diep D, Krauss S, Kozmik Z. Wnt-mediated down-regulation of Sp1 target genes by a transcriptional repressor Sp5. **J Biol Chem.** 2007;282:1225-37.
4. Jonášova K, Kozmik Z. Eye evolution: lens and cornea as an upgrade of animal visual system. **Semin Cell Dev Biol;** Epub Oct 13,2007.
5. Machon O, Backman M, Machonova O, Kozmik Z, Vacik T, Andersen L, Krauss S. A dynamic gradient of Wnt signaling controls initiation of neurogenesis in the mammalian cortex and cellular specification in the hippocampus. **Dev Biol.** 2007;311:223-37.



Sp5 gene is activated by canonical Wnt/β-catenin signalling (Fujimura et al., 2007).