



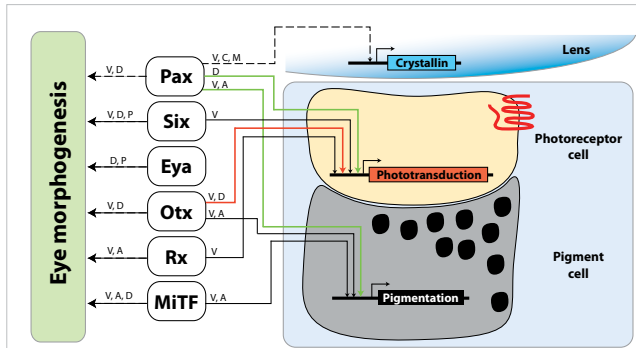
# Laboratory of Transcriptional Regulation

Eye development and evolution, Pax genes, Wnt/ $\beta$ -catenin signalling

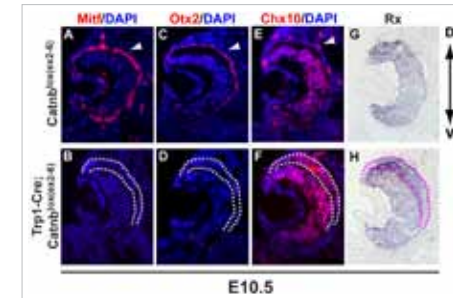
## Zbyněk Kozmik

zbynek.kozmik@img.cas.cz

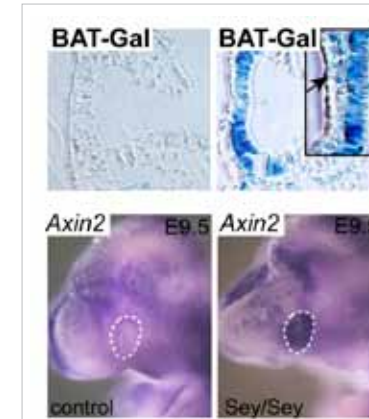
We are interested in the genetic basis of mammalian eye development. Our focus is on the role of transcription factors and signalling cascades, especially on the role of *Pax6* gene, Wnt/ $\beta$ -catenin signalling pathway and their genetic interaction. A combination of gain-of-function (transgenic) and loss-of-function [conditional knock-outs] approaches is used. Our second main interest is eye evolution. Early morphological studies have suggested that eye has evolved multiple times during the course of evolution. In contrast, more recent genetic data indicate a conserved role of *Pax6* and some other transcription factors in eye formation in a wide range of animals. In fact, eye assembly always relies on the same basic principle, i.e. photoreceptors located in the vicinity of dark shielding pigment. Several model systems including amphioxus, scallop, medaka and jellyfish are used in the laboratory to study various aspects of eye evolution.



**Fig. 1.** Dual role of transcription factors in regulation of both eye development and differentiation genes [Vopalensky and Kozmik, 2009].



**Fig. 2.** Elimination of Wnt/ $\beta$ -catenin signalling in the developing retinal pigment epithelium (RPE) leads to tissue hyperproliferation and transdifferentiation of RPE into neural retina. Please note the loss of RPE markers [Otx2, Mitf] and the gain of neural retina-specific markers [Chx10, Rx] [Fujimura et al., 2009].



**Fig. 3.** Wnt/ $\beta$ -catenin signalling is ectopically activated in Pax6-deficient [Sey/Sey] mouse embryos as exemplified by the upregulation of Wnt-sensitive reporter gene *BAT-gal* and Wnt target gene *Axin2* [Machon et al., 2010].



- AS CR, IAA500520604 – Developmental genetics of amphioxus: insight into evolutionary origin of vertebrates, 2006–2010, Z. Kozmik
- GA CR, GA204/08/1618 – Molecular basis of canonical Wnt signalling during eye and brain development, 2008–2010, Z. Kozmik
- GA CR, GD204/09/H058 – Intercellular signalling in development of the organism and disease, 2009–2012, Z. Kozmik
- AS CR, IAA500520908 – The role of Pax genes in eye evolution, 2009–2013, Z. Kozmik
- GA CR, GCP305/10/J064 – Reconstructing urbilaterian photoreceptors: comparative study between Branchiostoma [Chordata] and Platyneris [Annelida], 2010–2013, Z. Kozmik



1. Machon O, Kreslova J, Ruzickova J, Vacik T, Klimova L, Fujimura N, Lachova J, Kozmik Z. Lens morphogenesis is dependent on Pax6-mediated inhibition of the canonical Wnt/ $\beta$ -catenin signaling in the lens surface ectoderm. *Genesis* 2010 48(2): 86–95.
2. Ruzickova J, Piatigorsky J, Kozmik Z. Eye-specific expression of an ancestral jellyfish PaxB gene interferes with Pax6 function despite its conserved Pax6/Pax2 characteristics. *Int J Dev Biol* 2009 53(4): 469–482.
3. Fujimura N, Taketo MM, Mori M, Korinek V, Kozmik Z. Spatial and temporal regulation of Wnt/ $\beta$ -catenin signaling is essential for development of the retinal pigment epithelium. *Dev Biol* 2009 334(1): 31–45.
4. Vopalensky P, Kozmik Z. Eye evolution: common use and independent recruitment of genetic components. *Phil Trans R Soc Lond B Biol Sci* 2009 364(1531): 2819–2832.
5. Kozmik Z, Ruzickova J, Jonasova K, Matsumoto Y, Vopalensky P, Kozmikova J, Strnad H, Kawamura S, Piatigorsky J, Paces V, Vlcek C. Assembly of the cnidarian camera-type eye from vertebrate-like components. *Proc Natl Acad Sci USA* 2008 105(26): 8989–8993.



From left:  
Zbyněk Kozmik, PhD / Head of Laboratory  
Jiří Pergner, MSc / PhD Student (since 2010)  
Lucie Klímová, MSc / PhD Student  
Peter Fabian, MSc / PhD Student (since 2010)  
Jitka Láčková, MSc / Research Assistant  
Anna Zítová, MSc / Research Assistant  
Daniela Gurská / Diploma Student  
Pavel Vopálenský, PhD / Research Fellow  
Barbora Antošová / Diploma Student  
Jan Mašek, MSc / PhD Student (since 2010)  
Michaela Horejsková, MSc / PhD Student (since 2009)

Not on the picture:  
Naoko Dupačová, MSc / PhD Student (maternity leave)  
Kristýna Hradílková, MSc / PhD Student (until 2010)  
Iryna Kozmiková, MSc / PhD Student  
Romana Kučerová, PhD / Research Fellow  
Ondřej Machoň, PhD / Research Fellow  
Kristýna Mářková, MSc / Diploma Student (until 2009)  
Veronika Nosková / Research Assistant (since 2010)  
Barbora Pavlů, MSc / PhD Student (until 2010)  
Juraj Sekereš / Diploma Student (until 2009)  
Jana Smolíková, PhD / Research Fellow (until 2010)