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Carcinogenesis, cell differentiation, EGR4

Research topics

The research efforts of the group focus on genes and molecular mechanisms involved in 1) fate determination in multipotent haematopoietic and neural cells and terminal differentiation of haematopoietic, neural and myogenic cells; 2) malignant transformation of haematopoietic cells, melanocytes, nephrogenic blastema and lung cells; 3) apoptosis induced by photoactivation of specific porphyrins; 4) epithelial to mesenchymal and mesenchymal to epithelial transitions.

In studies on cell fate determination, differentiation and malignant transformation of haematopoietic and neural cells (collaboration with the Institute of Anatomy, Prague), c-*myb* and v-*myb* genes are used as tools to modulate development of avian cells and tissues. In studies on the nephrogenic blastema transformation and lung tumour formation, MAV retroviruses serve as tumour inductors in experimental chicks. Porphyrin derivatives synthesized by the cooperating group (Institute of Chemical Technology, Prague) are used for experiments with targeted drug delivery and induction of cell death in cancer cells and tissues. Finally, genes of egr and myb families serve as tools to affect epithelial and mesenchymal cell phenotypes.

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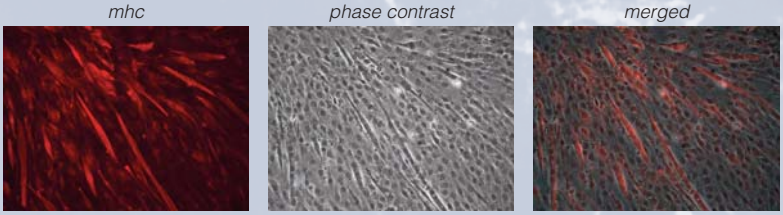
Selected recent papers

1. Kral V, Lang K, Kralova J, Dvorak M, Martasek P, Chin A, Andrievsky A, Lynch V, Sessler JL. Polyhydroxylated sapphyrins: multisite non-metallic catalysts for activated phosphodiester hydrolysis. **J Am Chem Soc.** 2006;128:432-437.
2. Kralova J, Synytsya A, Pouckova P, Koc M, Dvorak M, Kral V. Novel porphyrin conjugates with a potent photodynamic antitumor effect: differential efficacy of mono- and bis-β-cyclodextrin derivatives *in vitro* and *in vivo*. **Photochem Photobiol.** 2006;82:432-438.
3. Nanka O, Valášek P, Dvořáková M, Grim M. Experimental hypoxia and embryonic angiogenesis. **Dev Dyn.** 2006;235:723-733.
4. Pajer P, Pečenka V, Králová J, Karafiát V, Průková D, Zemanová Z, Kodet R, Dvořák M. Identification of potential human oncogenes by mapping the common viral integration sites in avian nephroblastoma. **Cancer Res.** 2006;66:78-86.
5. Karafiat V, Dvorakova M, Pajer P, Cermak V, Dvorak M. The melanocyte fate in neural crest is triggered by myb proteins through activation of c-kit. **Cell Mol Life Sci.** 2007;64:2975-2984.
6. Kaspar P, Dvorak M. Involvement of phosphatidylserine externalization in the down-regulation of c-myb expression in differentiating C2C12 cells. **Differentiation**. Epub Oct 9,2007.



Differentiation of myogenic cells to myotubes. Myosin heavy chain (mhc) expression (red fluorescence) in differentiating muscle cell line C2C12.

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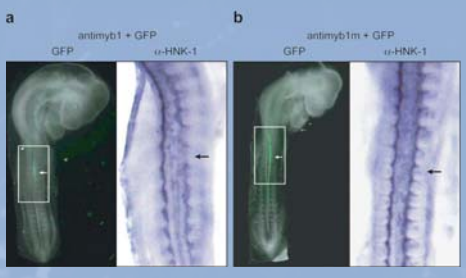
Detection of FoxP1 transcription factor (brown) in nuclei or cytoplasm of chicken nephroblastoma cells. Tissue microarrays were prepared from clonal tumours.



c-Myb is required for the formation of migratory neural crest cells. a) electroporated antimyb1 morpholino oligonucleotides reduce the amount of neural crest cells (detected by HNK-1 antibody - violet) emigrating from the neural tube of the chick embryo in the area depicted by the arrow. b) Control antimyb1m oligonucleotides have no inhibitory effect.