Laboratory of Molecular Virology

Carcinogenesis, cell differentiation, photodynamic therapy

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The recent research efforts of the group focus on genes and molecular mechanisms involved in 1) malignant transformation of haematopoietic cells, melanocytes, nephrogenic blastema, liver and lung cells; 2) metastasis and interactions between a tumour and its microenvironment; 3) fate determination in multipotent neural cells and differentiation of myogenic precursors; 4) apoptosis induced by photoactivation of specific porphyrins and development of porphyrin derivatives for potential use in photodynamic therapy. In studies on cell fate determination, differentiation and malignant transformation of haematopoietic and neural cells (collaboration with the Institute of Anatomy, Prague), *myb* genes are used as tools to modulate development of avian cells and tissues. In studies on genes involved in the formation of kidney, liver and lung tumours in chicks, insertional mutagenesis by MAV retroviruses is exploited. Genes of the *egr* family serve as tools to affect epithelial and mesenchymal cell phenotypes and metastatic potential of experimental tumours. 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.

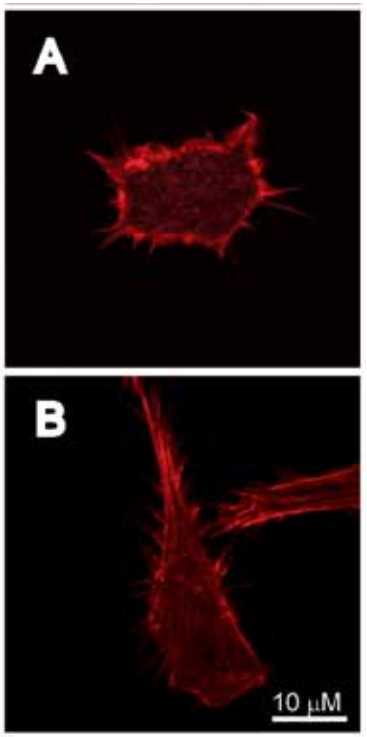

Fig. 1. Induction of the metastatic potential of the experimental tumour. The non-metastatic tumour cell (A) changes its phenotype (B) and acquires metastatic potential following Egr1 expression.

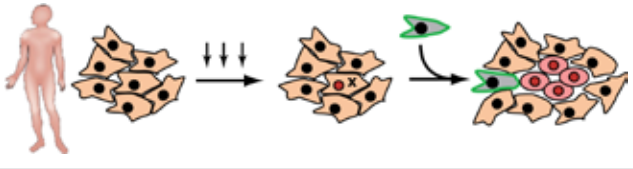

Fig. 2. The scheme of industasis – a previously unreported mechanism of promotion of malignant tumours. Tumour promotion has been very likely the trigger of the majority of human tumours. Tumour promotion consists of events capable of waking up a dormant incipient tumour cell (depicted by the cross) which has already accumulated genetic mutations (arrows) but remains under control of the surrounding microenvironment. It was found that normal non-malignant stray cells (green cell) can function as a tumour-promoting stimulus. We hypothesize that industasis might be the underlying cause of human multiple primary tumours.

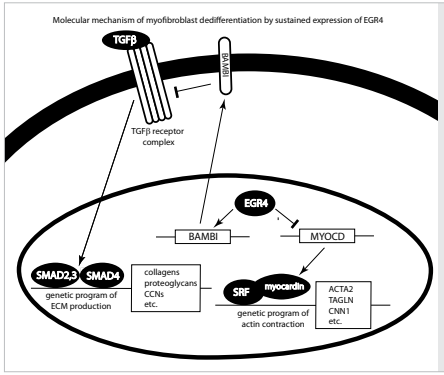

Fig. 3. Egr4 mechanism: The proposed mechanism of myofibroblast dedifferentiation by Egr4. We found that Egr4 both activates synthesis of BAMBI, the negative regulator of TGFβ signal, and blocks expression of myocardin, the gene necessary for the function of the cell contraction apparatus. In this way can Egr4 suppress those characteristics of myofibroblasts that support the onset of fibrosis.

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- AS CR, KAN200200651 – Nanoparticulate and supramolecular systems for targeted drug delivery, 2006-2010, J. Králová
- GA CR, GA301/09/1727 – Large-scale identification of genes responsible for the formation of solid tumours, 2009-2012, M. Dvořák
- GA CR, GA203/09/1311 – Synthetic probes for recognition of tumour markers: applications for cell directed apoptosis and targeted photodynamic therapy, 2009-2012, J. Králová
- GA CR, GAP305/10/2133 – The study of satellite cells migration, 2010-2012, P. Kašpar

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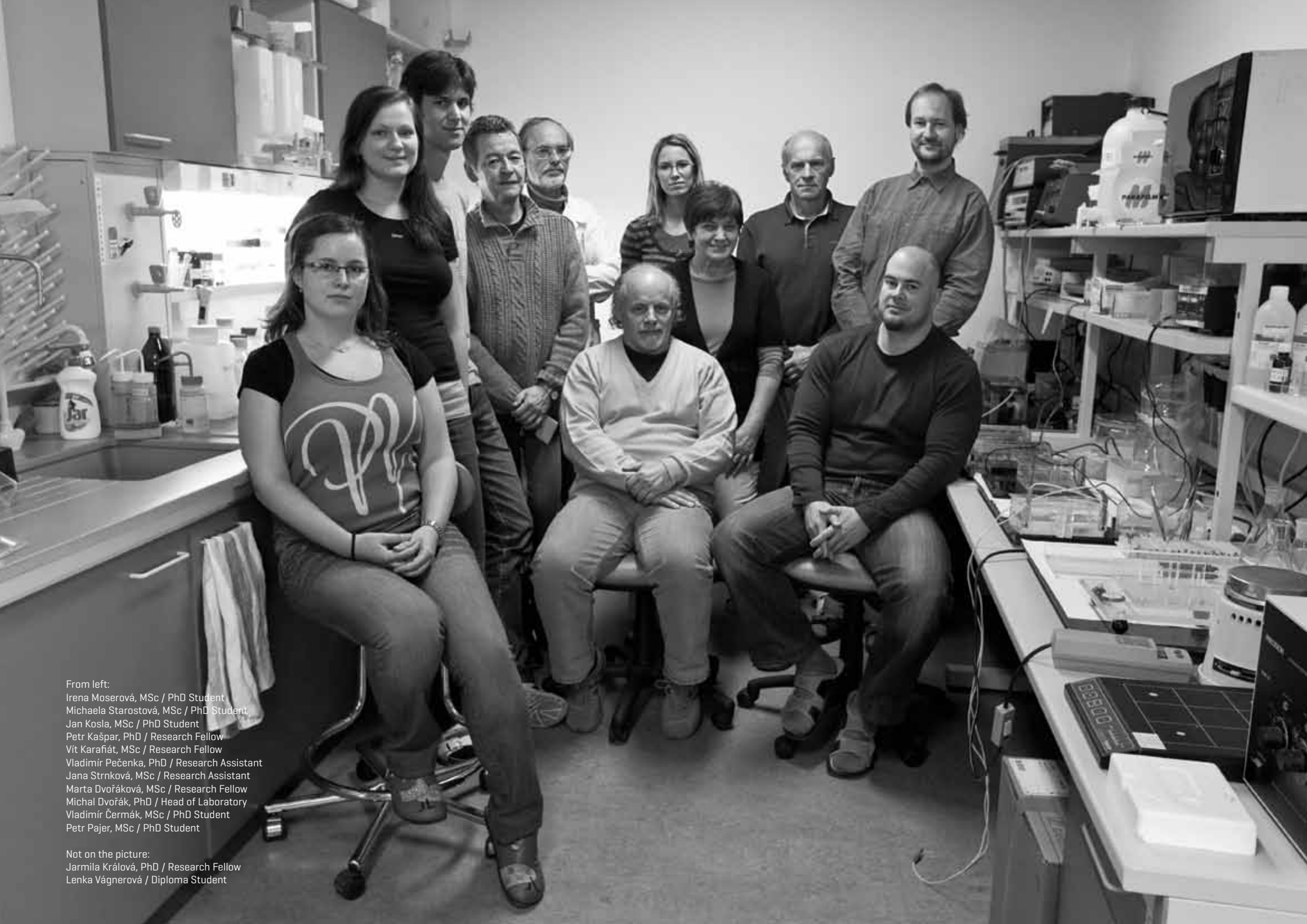

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