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CELL DIFFERENTIATION

haematopoietic and neural cell differentiation, zebrafish development, nuclear receptors, chemical biology

The main interest of the laboratory is study of the molecular mechanism of cell fate determination. We have established in vitro systems to get insight into the self-renewal and differentiation of haematopoietic and neural stem cells. Neural stem cells [NSCs] are defined by their dual ability to self-renew through mitotic cell division or differentiate into the varied neural cell types of the CNS. DISP3/PTCHD2 is a sterol-sensing domain-containing protein, highly expressed in neural tissues, whose expression is regulated by thyroid hormone. We demonstrated that NSC differentiation triggered significant reduction in DISP3 expression in the resulting astrocytes, neurons and oligodendrocytes. Moreover, when DISP3 expression was disrupted, the NSC "stemness" was suppressed, leading to a larger population of cells undergoing spontaneous neuronal differentiation. Conversely, overexpression of DISP3 resulted in increased NSC proliferation and impaired cell differentiation. Our findings imply that DISP3 may help dictate the NSC cell fate to either undergo self-renewal or switch to the terminal cell differentiation programme [Konirova et al. 2016]. We have extended our studies on vertebrate haematopoietic development to the zebrafish model and we have established ex vivo cultures of haematopoietic cells [Svoboda et al. 2016]. These studies brought information on how haematopoietic cytokines had evolved following the diversification of teleosts and mammals from a common ancestor. Moreover, these tools enabled us to reveal the clonogenic and proliferation capacity of multipotent progenitors with respect to their mammalian haematopoietic counterparts.

Selected recent papers:

Konirova J, Oltova J, Corlett A, Kopycinska J, Kolar M, Bartunek P, Zikova M: (2016) Modulated DISP3/PTCHD2 expression influences neural stem cell fate decisions. Sci Rep. 7: in press.

Svoboda O, Stachura DL, Machonova O, Zon L I, Traver D, Bartunek P: Ex vivo tools for the clonal analysis of zebrafish hematopoiesis, Nat Protocols. 2016; 11(5):1007-20.

Hron T, <u>Pajer P</u>, Paces J, <u>Bartunek P</u>, Elleder D: Hidden genes in birds. **Genome Biol. 2015**; 16:164-167.

