



LABORATORY OF

CELL DIFFERENTIATION

Hematopoietic cell development, signalling pathways, cytokines, small molecules, zebrafish, lamprey, chicken

Petr Bartůněk

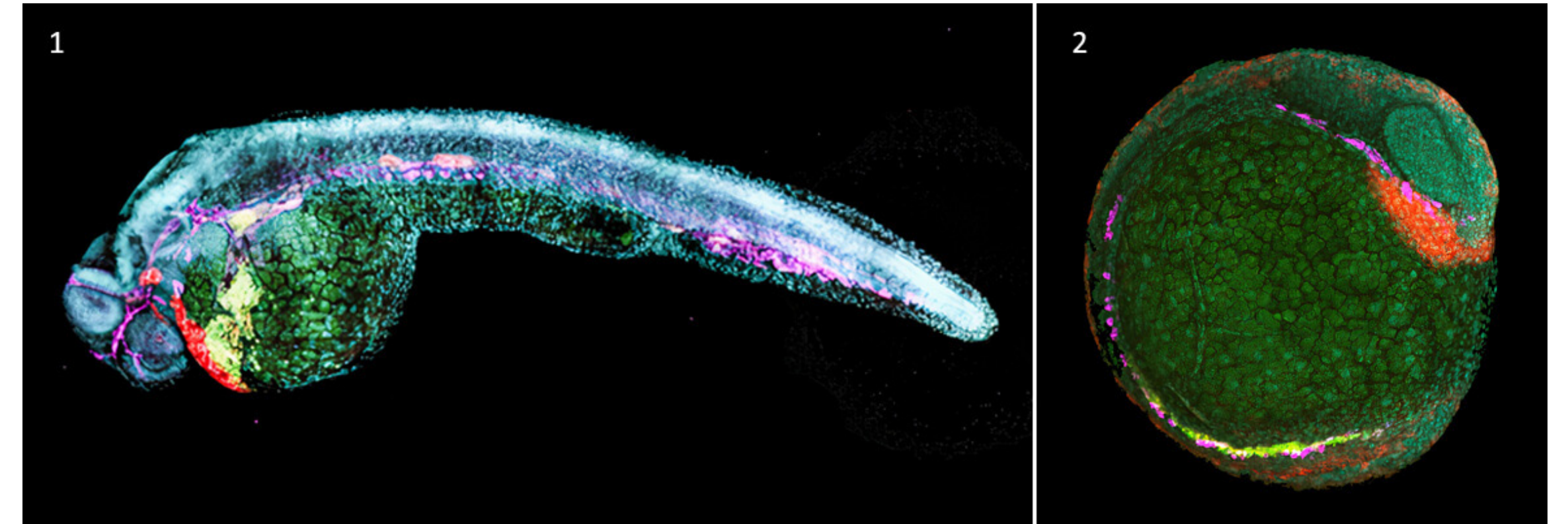


In the picture: 1. Dobiášovská Ivana | 2. Vondráková Zuzana | 3. Dvořáková Marta | 4. Hojerová Tereza | 5. Hingarová Tereza | 6. Jarošová Šárka | 7. Epp Allan Trevor | 8. Jovičić Jovana | 9. Maystorova Rositsa | 10. Blažka Martin | 11. Kovář Martin | 12. Dvořák Michal | 13. Machoňová Olga | 14. Svoboda Ondřej | 15. Zíková Martina | 16. Bartůněk Petr | 17. Schuster Björn

The main interest of the laboratory is to study the molecular mechanism of cell fate determination. We use cytokines/growth factors and small molecules as tools to manipulate hematopoietic cell fate in model organisms [zebrafish, lamprey, chicken, mouse] and human primary cells to gain insight into the mechanisms underlying self-renewal, proliferation and differentiation.

Zebrafish are suitable model organisms for modeling human disease and their small size makes them advantageous for high-throughput preclinical drug screening. We have developed a novel system for bioluminescent detection of transplanted cells that will accelerate the drug development process. For this purpose, we used the NanoLuc luciferase, which provided rapid quantification of tumor cell growth in vivo with high sensitivity and low background compared to conventional fluorescence measurements.

We also focused on M-CSFR/CSF1R signalling and the role of cytokines Csf1a, Csf1b and Il34 in zebrafish embryonic and adult hematopoiesis. We used a set of zebrafish loss-of-function mutants to discern the effects of functional defects in Csf1-receptors and -ligands. We show that Csf1a controls embryonic macrophage expansion and Il34, acting through Csf1rb, is important for embryonic granulopoiesis. We further studied the role of zebrafish Kit ligands in hematopoietic development and performed gain-of-function experiments in zebrafish embryos, which showed that both ligands cooperate with erythropoietin [Epo] in promoting erythroid cell expansion. This was further verified using ex vivo cultures of erythroid progenitors grown in suspension culture or semi-solid media. Thus, our studies clearly demonstrated that hematopoietic cytokine signalling is evolutionarily conserved from fish to humans.



Embryos were fixed at segmentation 8 somites stage [11.5 hpf] or pharyngula stage [30 hpf], respectively and stained using gata1a [green], klf17 [red] and etv2 [magenta] by Hybridisation Chain Reaction probes [HCR, Molecular instruments]. The nuclei were co-stained with DAPI [cyan]. In figure 1, the gata1a and klf17 positive primitive erythroid progenitors that are differentiating from early mesoderm are located in a caudal region within the inner cell mass and will enter circulation [figure 2] later on. Migrating endothelial vein and arterial progenitors are visualized by etv2 probe [figure 1] and will give rise to blood vessels [figure 2]. The klf17 positive structure at the anterior-ventral side of the yolk sac will develop into the hatching gland throughout subsequent development. Imaging was performed using Dragon fly [Andor] spinning disk.

Selected publications:

1. [Oltova J, Svoboda O, Machonova O, Svatonova P, Traver D, Kolar M, Bartunek P*](#). Zebrafish Kit ligands cooperate with erythropoietin to promote erythroid cell expansion. *Blood Adv.* 2020 Dec 8;4(23):5915-5924.
2. [Sedlak D, Wilson TA, Tjarks W, Radomska HS, Wang H, Kolla JN, Leśnikowski ZJ, Alena Spickakova, Ali T, Ishita K, Rakotondraibe LH, Vibhute S, Wang D, Anzenbacher P, Bennett C, Bartunek P*, Coss CC*](#). Structure-Activity Relationship of para-Carborane Selective Estrogen Receptor β Agonists. *J Med Chem* 2021 Jul 8;64(13):9330-9353.
3. [Hason M, Mikulasova T, Machonova O, Pombinho A, van Ham TJ, Irion U, Nüsslein-Volhard C, Bartunek P*, Svoboda P*](#). M-CSFR/CSF1R signaling regulates myeloid fates in zebrafish via distinct action of its receptors and ligands. *Blood Adv* 2022 Mar 8;6(5):1474-1488.
4. [Kralova K*, Popr M, Valecka J, Bartunek P](#). Sterolight as imaging tool to study sterol uptake, trafficking and efflux in living cells. *Sci Rep* 2022 Apr 15;12(1):6264.
5. [Hason M, Jovicic J, Vonkova I, Bojic M, Simon-Vermot T, White RM, Bartunek P*](#). Bioluminescent Zebrafish Transplantation Model for Drug Discovery. *Front Pharmacol* 2022 Apr 27;13:893655.