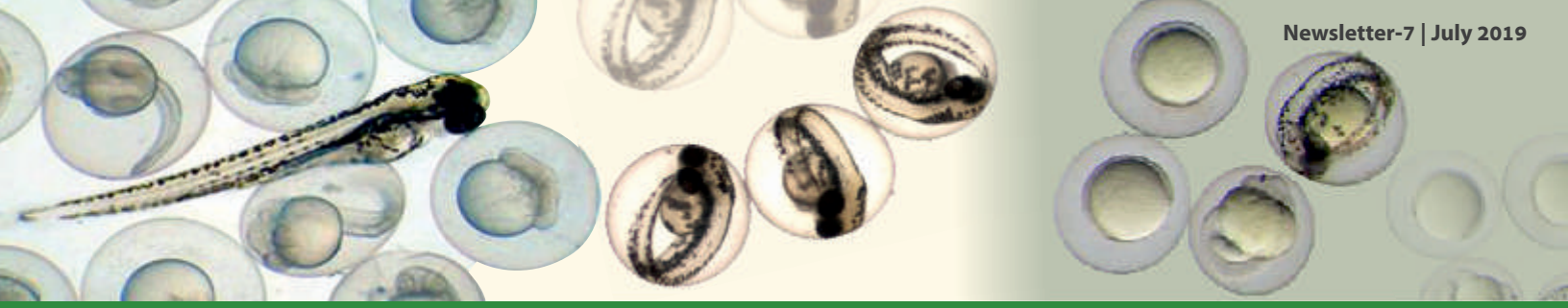


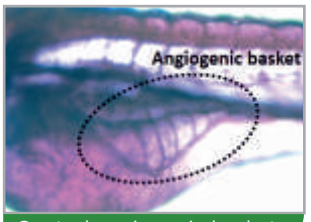
Zebrafish Embryo-Larvae: A High-Throughput Screening Model of Pro-Angiogenesis

Tumour angiogenesis is a key target area in cancer drug development. Evaluating the efficacy of novel angiogenic inhibitors require development of suitable animal models in which vasculature can be easily explored. Zebrafish, a vertebrate organism has proved to be a promising model in cancer research[1] .The optical transparency, highly characteristic blood-vessel patterning with short period of development (96 hour post fertilization; hpf) make the Zebrafish embryo-larvae best suited for vascular biology studies. Normal vasculature of Zebrafish embryo-larvae has been explored to screen anti-angiogenic compounds [2] Compared to normal vasculature, tumour induced vasculature shows profound morpho-functional modifications. Accurate efficacy of a drug can be reached by studying its effect on tumour angiogenic or pro-angiogenic model by examining the pattern and the molecular genetics leading to vascular normalization on drug exposure. Engrafting tumour cells into Zebrafish embryo-larvae (tumour xenograft) is a widely used technique to trigger angiogenesis[3]. It requires fluorescently labelled human cancer cells, skilled personnel and huge number of tumour xenografts for large scale screening. An easy and rapid alternate approach to induce pro-angiogenesis in Zebrafish embryo-larvae is discussed in this newsletter.

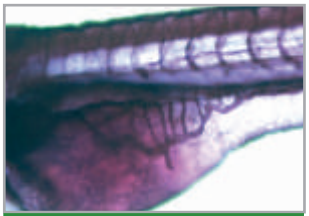
At JRF, we successfully developed pro-angiogenic model of Zebrafish embryo-larvae. We used known carcinogenic chemicals to induce pro-angiogenesis. Zebrafish embryos (24 hpf) were exposed to sub-lethal concentrations of the carcinogenic compounds along with appropriate control. At 96 hpf, the larvae were subjected to whole mount alkaline phosphatase staining allowing microscopic evaluation of two angiogenic parameters [number of sub-intestinal vessels (SIVs) and the vessel length][4]. As compared to the development of normal angiogenic basket formed in the dorsal-lateral part of the yolk in the control larvae, carcinogen treated Zebrafish larvae exhibited pro-angiogenesis which was evident by their potential to disrupt the angiogenic basket.

This Zebrafish efficacy-toxicity model of pro-angiogenesis can be employed as a high throughput screening tool for dual purpose. Firstly, to screen for pro-angiogenic / carcinogenic potential of compounds, resulting in selection of safer compounds entering the market as well as for cancer risk assessment of harmful pollutants. Secondly, the carcinogen induced pro-angiogenic model can be used to screen for potential anti-angiogenic compounds in cancer drug discovery.

Keywords: Zebrafish, Carcinogen, Pro-angiogenesis, Drug Discovery



Control angiogenic basket


Disrupted angiogenic basket

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Nilambari is a Senior Research Officer in the Ecotoxicology section. She has a good experience of conducting aquatic studies and is actively involved in research validations. She has professional experience of more than 11 years, including academic research, pharmaceutical R&D and CRO industry.

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