Editorial

The utility of zebrafish thrombosis models in determining the location of thrombus formation

Debkumar Chowdhury

Emergency and Urgent Care Department, Manchester Royal Infirmary, Manchester, UK

Correspondence to: Debkumar Chowdhury, MBChB, MSc Trauma, PGCert HPE, MAcadMEd, FRSPH. Emergency and Urgent Care Department, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, UK. Email: dc7740@my.bristol.ac.uk.

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Ischaemic stroke is associated with high rates of co-morbidities with resultant mortality if treatment is not administered in a timely manner. The pathophysiology of ischaemic stroke is thrombosis the location of which may be intravascular or intracardiac. The primary role of treatment is the identification of patients who have developed this particular form of stroke. The secondary role is that of stroke prevention while reducing the associated co-morbidities

In their study, Hwang *et al.* (1) evaluated thrombosis in both intracardiac and intracerebral models whilst inducing thrombosis in these models and then evaluated the activity of tissue plasminogen activator in these models. The study utilised zebrafish larvae in the thrombotic models. Through this study, the authors were able to highlight the two separate transgenic zebrafish thrombosis models in the context of thrombolysis with the use of tissue plasminogen activator (tPA). The eventual aim would be to utilise these models in the development of anti-thrombotic medications.

In the past transgenic mouse strains were utilised due to the availability of these animal models, however with time, there is a greater emphasis on the utility of transgenic zebrafish larvae over the past few years (2). The haemostasis associated with zebrafish is similar to that of mammalian coagulation thereby representing the continued use of this animal model (3). The coagulation profile and subsequently, thrombosis in the transgenic zebrafish model is similar to human studies, thus representing the continuing use therefore its utility in the localisation of thrombosis. However, there are two main differences between zebrafish and human models, the clotting times and the density of thrombocytes (4). It has been noted that the thrombocyte density is lower in zebrafish models in comparison to human models. In addition, the clotting times are shorter in zebrafish models than in animal models (1). Fish *et al.* (5) demonstrated how venous thrombosis was induced in zebrafish larvae through the use of laser injuries. Wang *et al.* (6) demonstrated the injection of thrombi directedly into the heart in male New Zealand white rabbits whilst highlighting no differences in heart structure or function.

Further on from the work carried out by Hwang *et al.* (1), it would be worth evaluating the results from this study on a large scale to ascertain the true impact of cost-effectiveness as well as assessing both the internal and external validity. As the authors have alluded the results from the study expand the horizon of the applicability of these two models in other clinical settings, highlighting the far-reaching implications. Clinicians may be better informed of a more directed therapy to the source of thrombosis. From my clinical practice, I would be interested in the impact of trauma on the formation of thrombosis during the hypercoagulable state (7). At the cellular level, the dysfunction of the endothelial glycocalyx forms the core of these disease processes (8). By undertaking future research,

the correlation between how thrombosis is created in animal models and the effect of anti-thrombotic medications can be evaluated further. Once the findings in the animal models have been sufficiently evaluated, the true impact of this can be studied in human models.

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