Unlocking the distribution of fluorescently labeled albumin in zebrafish

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The small size, translucent nature and ease of manipulation and observation as a whole, have made the zebrafish (*Danio rerio*) an increasingly attractive experimental model. However, only a few publications related to drug delivery into the zebrafish liver have been reported, resulting in limited information on the ultrastructural architecture and drug behavior/pathways. The efficacy of a therapeutic drug relies on the accumulation of the drug at the site of action at therapeutic levels. Hence, it is important to understand the behavior of prospective drugs to better tailor drug targeting studies and set a limit of confidence in the use of zebrafish as models for drug delivery studies.

The study presented herein reports on the drug carrier, albumin. Fluorescently-tagged albumin was injected into 12 days post-fertilisation zebrafish liver then, by applying correlative microscopy, functional and structural information were provided on the distribution of albumin in the zebrafish liver. Live confocal imaging was used to follow the albumin. At different time points, the zebrafish were fixed and processed for electron microscopy using a protocol whereby the fluorescence is retained. Sections across and throughout the liver were then imaged using both fluorescence- and electron microscopy. Correlation of the acquired data provided insights on the site of accumulation as well as respective rates of accumulation. Albumin was found to be accumulating within the liver sinusoidal endothelial cells as early as 5 min after injection. After 10 min, the accumulation rate stagnated and further incubation up to 15 min indicated post-uptake processing taking place at the cellular level.

The workflow established herein allowed to demonstrate the albumin pathway in zebrafish liver which is in line with that in rodents and human. This experiment forms the basis for future albumin-based drug-complexes experiments and validates the zebrafish as a suitable animal model for albumin-based drug delivery studies.