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Development of a novel anthraquinone-derived fluorescent lysosomal probe

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The lysosome presents a unique intracellular environment within the cell with a highly acidic lumen, containing several acid hydrolases. Partial or complete loss of function in one lysosomal hydrolase enzymes often leads to lipid accumulation, as well as an increase in the number of lysosomes and lysosomal volume. Lysosomal dysfunction is present in several diseases, including being the primary cause of over 50 lysosomal disorders. Therefore, the ability to visualise lysosomes is essential for both improving our understanding of diseases with lysosomal associated pathology and to develop drugs that improve lysosomal function. The recent development of small-molecule fluorescent probes has allowed ever increasing specific organelle staining and visualisation in-vitro. Currently the most commonly used family of lysosomal probes are the LysoTracker series of probes. However, the LysoTracker family of probes have several potential drawbacks to their use, including photobleaching, alkalinising lysosomes and cellular toxicity. Therefore, the creation of novel lysosomal probes, without the undesirable characteristics of LysoTracker dyes allows for increased imaging capabilities and assay potential. We have characterised a series of anthraquinone derivative lysosomal probes using high content imaging. The far-red fluorophore, AQ7, specifically localises to lysosomes, with no observable cellular toxicity at working concentrations. Additionally, we have shown that AQ7 fluorescence is pH sensitive, and can be used in-vitro to monitor lysosomal pH. AQ7 may be a superior live cell lysosomal marker for drug discovery than current commercially available lysosomal probes.