Fluorescent analogues of cholesterol for studying live-cell sterol trafficking

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Niemann-Pick type C disease is a neurodegenerative congenital disease, in which sterol trafficking, in particular in neural cells, is impaired. It is caused by mutations in two genes, NPC 1&2, which encode proteins vital in intracellular transport of cholesterol. While the general pathophysiology of the disease is known, many details of the underlying molecular mechanisms have not been elucidated yet[1].

Analysing live-cell trafficking of cholesterol and comparing it between control and NPC-affected cells is among the most important tools for studying these mechanisms. Fluorescence microscopy is the method of choice for such studies. However, cholesterol itself is not fluorescent, so its analogues have to be used for this purpose. One possible strategy is to attach a fluorophore moiety, such as BODIPY, to the cholesterol molecule[2]. This enables the use of fluorophores with the best parameters, such as quantum yield and emission wavelength. On the other hand, introducing them to a relatively small sterol molecule causes a significant change to its shape and structure. This can cause its properties to change drastically. In particular, it might no longer fit its carrier proteins. Therefore, it can be beneficial to convert cholesterol to an intrinsically fluorescent analogue by introducing a system of conjugated double bonds instead of relying on tagging approach. In my presentation, I will describe the synthesis, as well as benefits and drawbacks of such analogues. I will also present the results obtained from fluorescence microscopy studies performed on fibroblast cells labelled with intrinsically fluorescent sterol analogues[3].

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(3) Modzel, M.; Solanko, K. A.; Szomek, M.; Hansen, S. K.; Dupont, A.; Nåbo, L. J.; Kongsted, J.; Wüstner, D. Live-Cell Imaging of New Polyene Sterols for Improved Analysis of Intracellular Cholesterol Transport. *J. Microsc.* **2018**. https://doi.org/10.1111/jmi.12691.