Structural design of intrinsically fluorescent oxysterols.

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Oxysterols are oxidized derivatives of cholesterol with many important biological functions. Trafficking of oxysterols in and between cells is not well studied, largely due to the lack of appropriate oxysterol analogs. Intrinsically fluorescent oxysterols present a new route towards direct observation of intracellular oxysterol trafficking by fluorescence microscopy. We characterize the fluorescence properties of the existing fluorescent 25-hydroxycholesterol analog 25-hydroxycholestatrienol, and propose a new probe with an extended conjugated system. The location of both probes inside a membrane is analyzed and compared with that of 25-hydroxycholesterol using molecular dynamics simulations. The analogs' one- and two-photon absorption properties inside the membrane are evaluated using electronic structure calculations with polarizable embedding. Due to predicted keto–enol tautomerisation of the new oxysterol analog, we also evaluate the keto form. Both analogs are found to be good probe candidates for 25-hydroxycholesterol, provided that the new analog remains in the enol-form. Only the new analog with extended conjugated system shows significant two-photon absorption, which is strongly enhanced by the presence of the membrane.

Słowa kluczowe

Oxysterol, Fluorescence, Electronic structure calculation, Polarizable embedding, Imaging, Intracellular transport

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