

Fluorescent retinoids

Durham University and High Force Research Ltd. have developed a range of stable synthetic retinoids with strong intrinsic fluorescence. These molecules can function as both a biologically active retinoid and at the same time, act as imaging probes.

- Retinoids such as all-*trans*-retinoic acid (ATRA) are important signalling molecules that are involved in controlling many aspects of stem cell proliferation, differentiation and apoptosis.
- We developed synthetic, light stable ATRA analogue, EC23 to give highly reproducible stem cell differentiation.
- New analogues of EC23 have been designed which exhibit strong intrinsic fluorescence, whilst retaining the potent biological activity, *i.e.* DC360.
- DC360 enables unprecedented imaging of the cellular localisation of a retinoid using any fluorescence microscope (see the absorption and emission wavelengths shown below).
- Small molecule kit offered free of charge for research purposes, containing DC360 (a highly fluorescent analogue of EC23), DC461 (a "retinoid-like," fluorescent molecule, which is not biologically active), and EC23 which can be used as a non-fluorescent retinoid control and surrogate for ATRA.
- The three compounds (EC23, DC360 and DC461, shown below) will be supplied as pre-weighed solids which should be dissolved in either ethanol or dimethyl sulfoxide and used as other retinoids. Solutions are shelf-stable and can be handled under laboratory lighting without precaution.

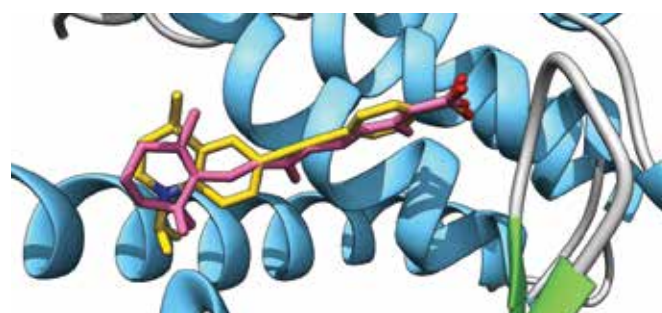


Figure 1: Docking simulation of a potential binding pose of DC360 (yellow) in RAR γ , calculated using GOLD, compared to that of ATRA (pink) determined by X-ray diffraction. The two binding poses are highly congruent, suggesting similar modes of action.

- The fluorescent retinoids can be imaged at treatment concentrations as low as 0.1 μ M. UV-A (340-380 nm) or violet excitation (405 nm) required; emission can be imaged in the blue/green (a DAPI filter set is ideal).
- Fluorescent retinoids have been tested on keratinocytes, neuroblastoma and teratoma cells.
- Exhibit the same biological activity as EC23.
- Localisation of fluorescent retinoids observed within test cells and zebra fish.

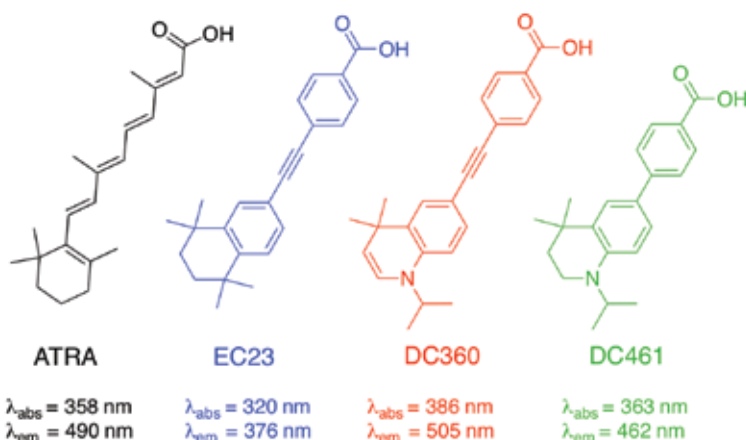


Figure 2: Endogenous retinoid ATRA, and available synthetic retinoids, EC23, DC360 and DC461. Emission and absorbance values relate to peak wavelengths recorded in chloroform.

REFERENCES

- [1] G. Clemens, K. R. Flower, P. Gardner, A. P. Henderson, J. P. Knowles, T. B. Marder, A. Whiting, S. A. Przyborski, *Mol. BioSyst.*, 2013, 3124 and references therein.
- [2] PCT/GB2015/052956

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