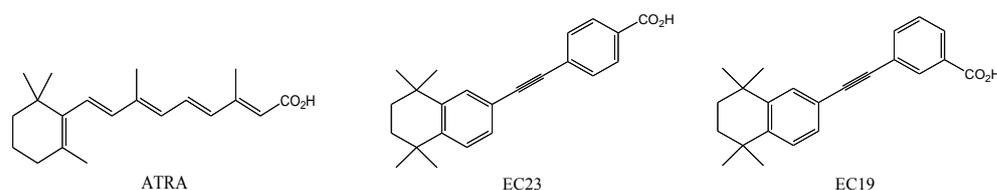


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Investigating the Differential Effects of Two Synthetic Retinoids *in vivo*. Rachel Lopez-Real

All-*trans* retinoic acid (ATRA) is essential for vertebrate development and is known to affect gene expression during embryogenesis. Incorrect levels of ATRA can induce serious teratogenic defects including craniofacial and limb malformations. Therefore, metabolism and availability of ATRA is tightly controlled *in vivo*. ATRA can isomerise upon exposure to light and these isomers may induce different effects compared to pure ATRA. Therefore, photostable analogues are advantageous for future research.



Two photostable, novel retinoids, EC23 and EC19 (above), can induce neural and epithelial differentiation respectively in cultures of human pluripotent stem cells (Christie, *Organic and Biomolecular Chemistry*, **6**; 3497, 2008). EC23 and EC19 have also been shown to generate differential effects *in vivo* (unpublished data summarised below). EC23 is more toxic than either EC19 or ATRA. Both synthetic retinoids can generate malformations as can ATRA (Figure) when applied to a S20 chick wing bud. EC23 is more potent than EC19 as it generates more extensive digit duplications at a higher frequency. EC19 also generates a different facial phenotype. Current work is to investigate the mechanism for the increased potency of EC23 and the receptors which these retinoids activate. Preliminary data suggests that EC23 is more potent than ATRA as it is more resistant to metabolism. Differential receptor activation has been investigated by determining the distribution of the retinoic acid receptors *in vivo*. Future work will involve further characterisation of these retinoids and their transcriptional targets *in vivo*.

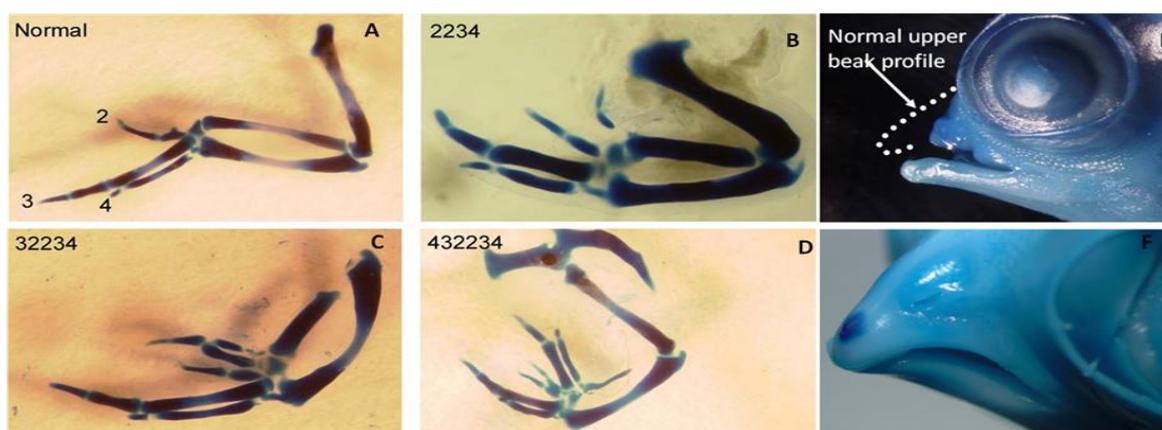


Figure – The differential effects of EC19 and EC23 *in vivo*. A) control limb exposed to DMSO stained with Alcian Blue and Alizarin Red with normal digits (234); ; B-D) range of digit duplications obtained with 0.01mg/ml EC23. The numbers indicate the digit patterns seen. E) and F) facial phenotype produced with 0.01mg/ml EC23 and 0.1mg/ml EC19, respectively.