ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

STRUCTURE-BASED DESIGN OF TRIFAROTENE (CD5789), A POTENT AND SELECTIVE RARγ AGONIST FOR THE TREATMENT OF ACNE

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Introduction: Retinoids have a dominant role in topical acne therapy and to date, only RARβ and RARγ dual agonists have reached the market.

Objectives: to confirm the hypothesis that developing RARγ –selective agonists could yield a new generation of topical acne treatments that would increase safety margins while maintaining the robust efficacy of previous drugs.

Materials and Methods: Structural knowledge derived from the X-Ray structure of known RARγ–selective molecule. Design, synthesis and in vitro evaluation of a novel triaryl series of RARγ agonists were performed including structure activity and property relationship.

Results: Results revealed an unique and isotype specific pocket in the RARγ ligand binding domain thus enabling the optimization of a novel triaryl series of RARγ selective agonist for topical administration.

Conclusions: Structural information led to the discovery of Trifarotene, a new RARγ –selective agonist as a potential new generation of topical acne treatments.