

## **Photodynamic therapy and adapalene in dermatology: synergistic effects in immortal human keratinocytes**

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We compared the effects of methyl levulinate (MAL)/photodynamic therapy (PDT) and adapalene, evaluated singly, versus combination therapy on HaCaT keratinocytes. Our aim was to determine whether the additive/synergistic outcomes of combination treatment were such that doses of each component could be reduced without affecting treatment efficacy. The analysis of data from specific PDT/adapalene combinations results indicating effects ranging from additive to clearly synergistic. We first evaluated the effects on cell viability, cell cycle and protein expression profiles of each individual treatment, then we tried to understand the reasons and the mechanisms whereby cells under combined treatment move more efficiently to death. Although we observed therapeutic strengthening by increasing either drug doses or light fluences, reinforcement was particularly marked in combinations in which PDT was predominant. Thus, if PDT is appropriately tuned, the dose of the drug can be reduced without compromising the therapeutic response. As both photodynamic therapy and adapalene have been and are therapeutic approaches to treat different dermatological pathologies such as acne, actinic keratosis etc., our data suggest that the adapalene-PDT combination may have important spin-off in clinical dermatology as a strategy to tackle this nasty condition.