

Antiandrogen oligonucleotides: active principles in hair- and skin-derived culture cells.

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Most drugs used for treatment of androgen-related dermatological disorders are not completely satisfactory in terms of clinical efficacy and potential secondary effects. There is, therefore, a need for a new generation of specific antiandrogens. This paper focuses on an oligonucleotide antisense pharmacological strategy. Acceptor sites were first disclosed by mapping the human Androgen Receptor (AR) mRNA conformation using an mRNA walking approach, oligonucleotide binding, and S1 protection assays. Antisense-sensitive regions were localized by RNase H degradation and AR in vitro translation inhibition. Oligonucleotides were then designed and assessed, in primary cultures of human hair dermal papillae and skin derived fibroblasts, for their capability to down-regulate AR expression. Some of them were able to inhibit more than 60 to 80% of the AR expression. These could be a new class of antiandrogen oligonucleotides pharmacologically active in hair and skin derived cells, suitable for the treatment of dermatological disorders.