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Functional Genomics in Baldness Research: Target Molecules for Development of Anti-alopecia Drug through cDNA Microarray Analysis

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Male pattern baldness is a gradual balding of the scalp which occurs commonly in men. The gradual transformation of terminal hair follicles producing large, thick, pigmented hairs, to smaller vellus ones forming short, thin non-pigmented hairs, with a much shorter growth period (anagen), occurs in a precise, well defined pattern, and is believed to require both androgens and the appropriate genetic tendency. This is supported by the absence of any frontal recession in XY individuals with complete androgen insensitivity, i.e. lacking functional androgen receptors. Apart from this requirement for circulating androgens and appropriate receptors within the follicle cells, little is known about the cell biological or molecular mechanisms involved, meaning that very little treatment is currently available except for corrective transplants. The success of such transplants, and the varying responses of hair follicles to androgens depending on their body site, indicating that the mechanisms involved depend on factors within the specific follicles.

The dermal papilla lies at the base of hair follicle and is composed of mesenchymal cells. The dermal papilla is thought to organize, direct, and maintain the function of a follicle, just as papillary dermis does the epidermis. In embryonic life a papilla induces a follicle to differentiate, and in post-uterine life it orchestrates the cycles of a follicle from growing through involutional to resting. The cells of the papilla are enmeshed in a dense extracellular matrix which undergoes extensive changes in concert with the hair cycle. Little is known of the biology of the dermal papilla which, although presumptive fibroblasts, are at least morphologically distinct from those of the dermis.

Identification of the genes that are specifically expressed in frontal dermal papilla cells but not in occipital dermal papilla cells(baldness genes), or vice versa, is important for understanding the molecular basis of male-type baldness. DD-PCR was applied to compare mRNAs from frontal dermal papilla and occipital papilla cells, cultured under the same conditions. cDNA fragments

corresponding to apparently differentially expressed mRNAs were recovered and sequenced.

The dermal papilla cDNA collection can provide a unique source of genes for genetic studies of male pattern baldness and hirsuitism as well as for molecular studies of epithelial-mesenchymal interaction, morphogenesis, growth, development, differentiation, apoptosis, hormone action and cyclical control of organ function. Thus, human dermal papilla cell cDNA library was constructed and a cDNA sequencing project was initiated to characterize gene expression in human dermal papilla.

The tool of microarray analysis has recently been developed as a very efficient means of studying the differential expression of many genes simultaneously. We have used microarrays containing 3,000 cDNAs from dermal papilla cells to investigate gene expression patterns in various conditions.