Project Title: Collective mechanism of hair regrowth during Alopecia Areata resolution
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Alopecia areata (AA) is a hair loss disorder caused by an autoimmune attack on the hair follicle. Hair loss can range from small patches of scalp hair loss to total scalp (alopecia totalis) or total body hair loss (alopecia universalis). Genetic factors are thought to play a part in the development of AA, however the exact mechanism behind the disease is not completely understood. One of the key components of AA is over-activity of immune cells. This process is mediated by an intracellular protein, Janus Kinase (JAK), which promotes continuation of the disease process. Given this discovery, JAKs have emerged as highly-effective therapeutic targets for the treatment of AA.

Consistent with evidence from the literature, many of our AA patients show strong hair regrowth in response to JAK inhibitors. Clinical observation has noted that hair regrowth occurs in patches that enlarge over time. This pattern of hair regrowth has been documented in multiple published studies, however not yet explicitly analyzed in humans. This "spreading wave" pattern of hair regrowth is strikingly similar to physiological hair regrowth observed in mice, rats, and rabbits; whereas early-stage, actively growing hair follicles signal to their neighboring quiescent hair follicles to rapidly enter the growth phase. Such a collective, chain reaction-like mechanism is very efficient and results in expanding and merging hair patches. In mice, the mechanism behind hair regrowth involves multiple growth factors produced by hair follicle cells, as well as other cells within the skin surrounding the hair follicle.

Here, we propose that adult human hairs are, in principle, capable of activation of a collective chain reaction-like hair growth pattern similar to mice. While this ability is not normally apparent in the healthy scalp, it can be obvious during AA resolution, a distinct disease state containing many quiescent hair follicles. The first objective of this pilot grant is to collect strong clinical proof for a "spreading wave" pattern of hair regrowth in AA patients. This will be accomplished by non-invasively imaging the hair follicles on the edges of re-growing hair patches. The focus will be on identifying the spatial arrangement of quiescent hair follicles to early growing hair follicles - a telltale sign of spreading hair regrowth waves. This will then be confirmed on histology with biopsies of hair patch edges. For the first time, this data will provide direct support for the ability of human scalp hair follicles to collectively enter the regrowth phase - a fundamentally new knowledge for the field of human hair and AA research. The second objective of this project is to collect RNA sequencing data from the edges of regrowing hair patches to identify novel signaling changes within the hair follicles and surrounding cells. These changes will include proteins that influence hair follicles to initiate regrowth, and thus are potential therapeutic targets for hair growth stimulation. We anticipate that our findings will lead to the development of new strategies for the treatment of AA; with the potential for the discovery of break-through therapies for additional types of hair loss.