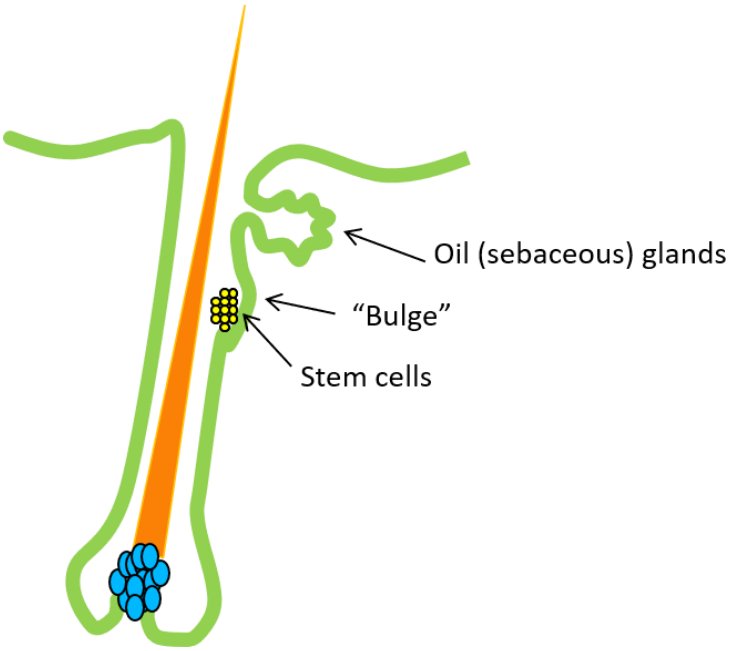
What is Causing this Condition?

Jeff Donovan, MD, PhD, FRCPC presented on this topic at the 2018 Patient Conference in Philadelphia. Dr. Donovan is a dermatologist, specializing in Hair Loss from Vancouver, Canada.

Determining what the cause of cicatricial alopecia is a multi-step approach that includes asking the patient questions about their symptoms, examining the scalp up close and looking at biopsy samples under a microscope. New technologies are now allowing us to identify additional changes inside cells that will someday point to specific causes of these diseases. Those changes can be in the genes, proteins or lipids.

Before going any further, it is important to understand the parts of the hair follicle.



The **Hair Shaft** is the part of the hair seen above the skin. It is made up of keratin and binding material, along with small amounts of water.

"Bulge" – located in the upper part of the hair follicle, houses the stem cells

Oil Glands/ Sebaceous Glands

Stem Cells

From looking under a microscope, we can find some clues as to what is causing scarring alopecia.

Clue 1: Most scarring alopecias have inflammation in the upper part of the hair follicle. This inflammation leads to the stem cells being destroyed. It's important to note that all types of cicatricial alopecia are associated with the destruction of hair follicle stem cells. In alopecia areata, a completely different type of hair loss with the potential for regrowth, the inflammation occurs at the bottom of the hair shaft, and the stem cells are not destroyed.

Clue 2: All scarring alopecias show loss of the sebaceous glands. Researchers, including Dr. Kurt Stenn, studied the role of oil glands. Dr. Stenn showed that the sebaceous glad is needed for normal hair functioning. Early mouse models showed that mice with mutations in the sebaceous gland developed scarring alopecia. Studies have also shown that some of the very earliest changes in scarring alopecia occur in the sebaceous glands. However, these studies did not have any clues as to what early events caused the loss of sebaceous glands, inflammation and the loss of stem cells.

In 2008, Dr. Pratima Karnik compared scalp biopsies from patients with LPP to those without LPP. They found receptors (PPAR Gamma) controlling lipid metabolism were significantly downregulated in LPP. They also showed that altered (proinflammatory, toxic) lipids are important to how scarring alopecia develops.

Observations from Scalp Biopsies of Patients with Different Stages of LPP

No LPP	Early LPP	Active LPP
No inflammation	Mild inflammation	Dense Inflammation
Well-formed sebaceous gland	Loss of some sebaceous glands	Loss of Sebaceous Gland
	Only a few inflammatory genes upregulated	Lots of inflammatory genes upregulated
	Lipid genes extremely down regulated	
	Decreased PPAR by 27 fold	Decreased PPAR by 19 fold

PPARS nuclear receptor proteins have many responsibilities throughout the body, including the control of inflammation, scarring and blood sugars. They also control fat cells and lipid metabolism. However, when they stop communicating with the nucleus, it leads to abnormal inflammation, scarring, blood sugar and lipid metabolism.

In terms of how this plays into the chain reaction that causes cicatricial alopecia, we know that reduced PPAR Gamma leads to proinflammatory lipids when then causes the loss of sebaceous glands, inflammation and loss of stem cells. However, researchers are still investigating what triggers this chain reaction to occur. Does environment or genetics play a role?

According to Dr. Donovan, the next era of research will look to see if we can pinpoint more details about potential triggers. The new technologies of lipidomics, proteomics and genomics will undoubtedly have an important role in advancing our knowledge. What role, if any, does genetics have? What lipid changes are most important? How can we block these changes in lipid alteration, sebaceous gland atrophy and stem cell depletion/dysfunction?