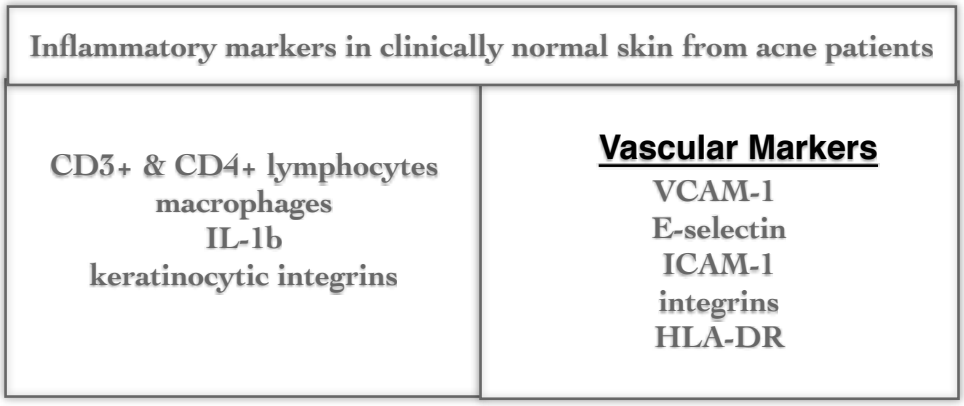
Acne Pathogenesis

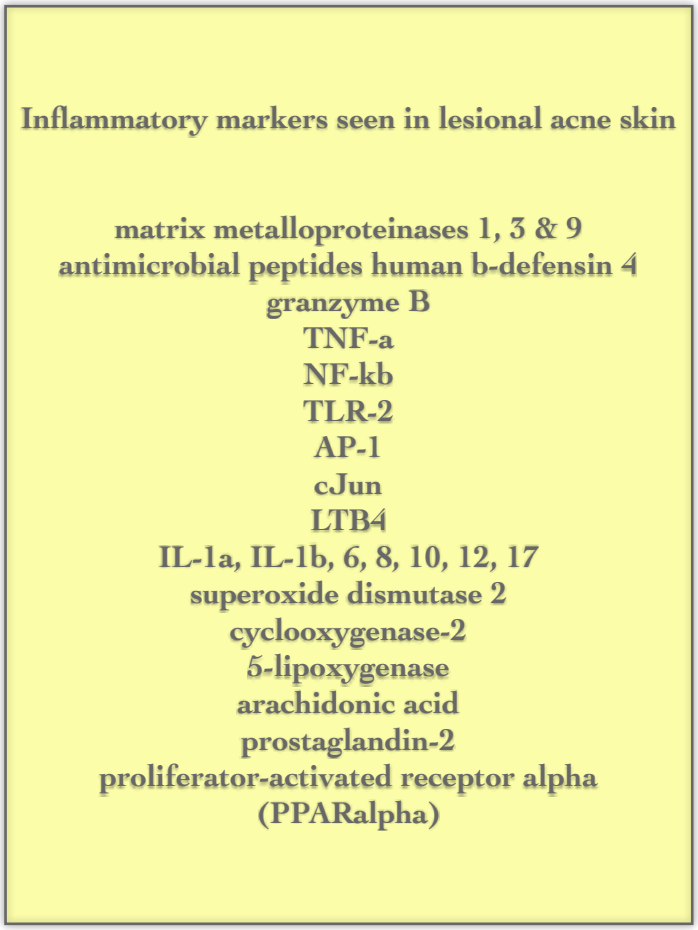
The pathophysiology of acne has for the most part centered around the formation of the microcomedone. Follicular hyperkeratinization, increased sebum production and the proliferation of Propionibacterium acnes combine to form the microcomedone with its eventual rupture and associated inflammation.

Studies done over the last fifteen years have suggested that acne is primarily an inflammatory disease with changes to the folliculosebaceous unit as a secondary event. When clinically normal follicles from acne patients were compared to patients without acne using immunohistochemical techniques, the only significant difference was the presence of inflammation in the acne patients. Features of hyperkeratinization and microcomedone formation were absent. Numerous characteristics of inflammation in clinically normal skin were present in the perifollicular and paillary dermis of acne patients, including an increased number of macrophages and lymphocytes, as well as a diverse array of inflammatory cytokines.

In addition to inflammatory mediators, an upregulation of angiogenesis is indicated by the increase in vascular-αv-integrin and HLA-DR. Epidermal integrin expression was also increased. Integrins are one type transmembrane protein involved in the adhesion of cells to the extracellular matrix and to each other.



The evidence for acne as an inflammmatory disorder becomes even more compelling when one examines the list of inflammatory mediators seen in acne lesions.

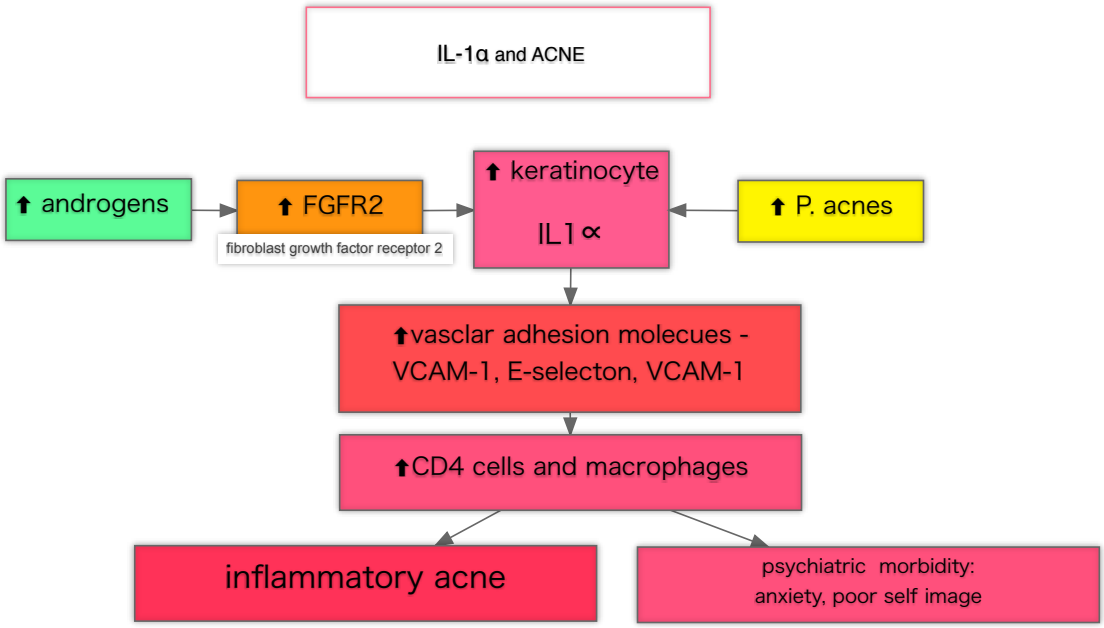


Toll-like receptors (TLRs) 2 and 4 are the switches for turning on the innate immune system and starting the inflammatory cascades that is a major contributing factor leading to the development of acne.

IL-8 is a neutrophilic chemotactic factor. TNFa activates transcription factor NFkb which induces keratinocytic production of cytokines, chemokines, and reactive oxygen species.

P. acnes is capable of stimulating IL-1α production from keratinocytes in vitro. The importance of IL-1α in acne development includes the demonstration of its ability to induce keratinocytic hypercornification in vitro, which can be mitigated by blockade of the IL-1 receptors. Skin biopsies of acne vulgaris lesions contained higher amounts of IL-1α when compared to controls. MABp1, a human antibody that specifically targets

IL-1α, has recently shown efficacy in a clinical trial. MABp1 not only reduced inflammatory acne lesion counts, but also attenuated acne's psychological comorbidities. Acne and its psychological comorbidities are know to share many of the same inflammatory mechanisms and related nutritional deficiencies.



A sequential digital photographic study of patients with untreated facial acne over a 12 week period revealed that 28% of inflammatory acne lesions occurred de novo on normal-appearing skin without evidence a preexisting comedone. This further lends support to the new paradigm that acne is an inflammatory disease at all stages, from subclinical evolution to overt expression.