**Halt the hedgehog**

Basal cell carcinoma (BCC), the most common skin cancer in the United States, is associated with mutations that activate the hedgehog signaling pathway to mediate unchecked proliferation of basal cells. A phase I trial was performed to evaluate the effects of daily treatment with GDC-0449, a selective hedgehog pathway inhibitor with notable antitumor activity, on patients with metastatic or locally advanced BCCs that were not amenable to typical surgical, radio-, or systemic therapies. Eighteen of the 33 enrolled patients responded to GDC-0449 treatment. No grade 5 adverse effects and only one grade 4 adverse effect were reported. High mRNA expression of the transcription factor GLI1, which induces hedgehog target genes, was observed in tumors from these patients. Taken together, these results support the notion that activation of the hedgehog pathway is critical for the growth and maintenance of advanced BCC. (N Engl J Med 361:1164–72, 2009)

**Information cascade**

Using data regarding the claim that β-amyloid, which is involved in brain injury in Alzheimer’s disease, is also produced by and injures skeletal muscle fibers in patients with sporadic inclusion body myositis, Steven Greenberg conducted an analysis of the citation network and the use of these references to solidify belief in these scientific claims. The 242 papers and 675 citations addressing this belief were combined to generate a network of 220,553 supporting citation paths. Using computational methods, four primary data papers, five model papers, and one review that supported this claim were identified as the most authoritative publications. Interestingly, six data papers that refuted this claim received little or no citation activity (only 6% of the citation activity). In perpetuating this information cascade, primary data that weakened or refuted the claims were ignored (citation bias), some influential papers and citations were exponentially cited (amplification), and related claims were issued as fact (invention). These citation distortions resulted in acceptance of this belief according to social network theory. (BMJ 339:b2680, 2009)

**Chemokine target for psoriasis treatment**

Although psoriasis is one of the most common immunemediated chronic inflammatory skin disorders, its underlying autoimmune mechanisms are far from clear. Psoriatic skin lesions exhibit high levels of IL-23, which functions as a key differentiation and growth factor for Th17 cells. In support of a role for the IL-23/Th17 axis in psoriasis, injection of IL-23 into mice induces some psoriasiform changes, although not all the aspects of human disease are replicated by this model. Hedrick and colleagues discovered that the chemokine receptor CCR6 is required for psoriasiform inflammation induced by intradermal injection of IL-23. Surprisingly, this inflammation did not occur via a direct effect on T cells but rather via a T-cell-independent inflammatory response. These results support therapeutic targeting of this chemokine receptor in Th17-driven diseases, especially because blockade of a chemokine receptor may actually cause less overall immunosuppression than broad-spectrum immune modulators. (J Clin Invest 119:2317–29, 2009)

**Another source of melanocytes**

During development, melanocytes are thought to arise from neural crest cells (NCCs) from the neural tube. These NCCs acquire a melanocyte fate, migrate dorsolaterally to populate the epidermis, and expand to generate 5–10% of the epidermal cells. In addition to confirming this model, Adameyko and colleagues demonstrated that large numbers of melanocytes are produced from nerves that innervate the skin. Specifically, the emergence of melanocytes is associated with Schwann cell precursors (SCPs). A strong correlation between nerves and Schwann cell phenotypes indicated that cells in contact with nerves retained an SCP state and eventually differentiated into Schwann cells, whereas cells that detached from the nerve acquired Mitf expression, which is indicative of the melanocyte lineage. Neuregulin and soluble signals, including insulin-like growth factor and platelet-derived growth factor, function via competing signals to instruct differentiation of SCPs toward Schwann cells or melanocytes. Thus, these results implicate SCPs as an additional cellular origin of melanocytes. (Cell 139:366–79, 2009)

**Dichotomy between benign and malignant**

Quite often, clinically benign tumors fail to progress to malignant tumors for reasons that have not yet been elucidated. Recently, Mandinova and colleagues compared the gene expression profiles of benign seborrheic keratoses (SKs) and malignant squamous cell carcinomas (SCCs). The tyrosine kinase receptor fibroblast growth factor receptor-3 (FGFR3) and the transcription factor forkhead box N1 (FOXN1) were upregulated in SKs and suppressed in SCCs. A positive feedback loop in which activating mutations of FGFR3 induce FOXN1 expression, which then leads to increased FGFR3 expression, locks the keratinocytes into a differentiation mode and prevents malignant transformation. This positive regulatory loop, therefore, underlies the dichotomy between benign and malignant tumor phenotypes in skin. This model suggests that shifting the gene expression patterns of malignant tumors toward that of benign lesions may be therapeutically beneficial. (J Clin Invest 119:3127–37, 2009)