Over the past decade, the hedgehog (HH) pathway has been found to be altered in patients with both syndromic and sporadic basal cell carcinoma (BCC) (Rohatgi and Scott, 2007). This pathway, when regulated, controls cell growth; however, alteration of the pathway results in cancer due to failure of patched 1, a component of the HH pathway, to suppress the protein Smoothened (SMO), which leads to uncontrolled cell growth and BCC development. Thus, ways to manipulate this pathway have been conceptualized. A systemically administered (oral) specific SMO inhibitor has been used for locally advanced or metastatic BCCs and shown to produce an overall response rate of 55% (Von Hoff et al., 2009).

Despite these responses, obstacles to systemic treatment exist. For example, because activation of the HH pathway plays an important role in the hair growth cycle, hair growth inhibition (alopecia) resulted upon systemic treatment of BCC. Therefore, a more desirable delivery system may be topical application of an SMO antagonist. Because BCC is the most common cancer in the United States and is increasing in prevalence and cost, novel treatments for BCC are of substantial interest. Skvara and colleagues (2011, this issue) studied a topical SMO antagonist, LDE225, to determine (i) whether this agent affects BCC growth in vitro, (ii) whether topical delivery of this agent is feasible, and (iii) whether the topical SMO antagonist would be well tolerated in patients and have a positive effect on BCC.

These investigators found that topical application of an SMO antagonist is feasible and led to inhibition of basaloid nest formation in vitro and murine hair growth in vivo. Application of this SMO antagonist to BCCs in patients with nevoid BCC syndrome was found to affect HH pathway activation and clinically reduced the size of the cancers in almost all cases. Through the following questions, we examine this paper in greater detail. For brief answers, please refer to the supplementary information online <http://www.nature.com/jid/journal/v131/n8/supplinfo/jid2011199s1.html>.

REFERENCES

QUESTIONS
1. What is nevoid basal cell carcinoma syndrome?
2. What studies were performed prior to a human trial with the topical medication?
3. How did the investigators study the medication in patients?
4. What were the results?
5. What did the investigators conclude?