Keratinocyte Growth Factor:
Reducing Costs and Increasing the Quality of Life for Cancer Patients

This is a story of how an intriguing development in a research laboratory many years ago ended up improving the quality of life for cancer patients undergoing treatment -- often nearly as important as the therapy itself.

Oral mucositis (painful sores and ulcers in the lining of the mouth) is a common side effect of many types of cancer therapies. Chemotherapy and radiotherapy both target and destroy rapidly dividing tumor cells, which also results in major damage to the rapidly dividing tissues that compromise the cells lining the mouth and throat. Oral mucositis can be extremely painful and can have a devastating impact on patients. It can make patients' everyday activities, such as eating, drinking, swallowing, and talking, difficult or impossible. Patients suffering from these debilitating mouth sores may require longer hospitalization, high doses of narcotics such as morphine, and intravenous feeding to receive nutrition and maintain hydration.

Until recently, there were no approved drugs available to prevent oral mucositis. Discovery of keratinocyte growth factor (KGF) led to a breakthrough in this field, a first of its kind demonstrating a clinically meaningful benefit in preventing or curing oral mucositis[1,2]. Palifermin, a man-made version of KGF, like the natural KGF, stimulates cells on the surface layer of the mouth to grow. This is thought to lead to faster replacement of these cells when killed by cancer treatments and is believed to speed up the healing process of mouth ulcers.

The motivation that led to the discovery of KGF resided in the conventional wisdom at that time that many cancers owe their origins and growth to hormones and growth factors. In 1989, NIH scientists (Rubin, et al) discovered a growth factor that they named KGF[3]. However, contrary to its hypothesized role, it was soon becoming clear that KGF was not the villain promoting tumors. Its unique sequence and high degree of specificity to epithelial cells led the inventors to file an invention report. At that time, KGF seemed a very promising molecule with several possible medical applications. The scientists appreciated that publishing their results would assist public health at one level, but seeking patent protection was important because it could open doors for eventual use in patients. Neither the inventors nor the licensees knew at that time which direction the clinical development of the molecule would take them. It took almost 16 years of commitment, hard work, persistence, and ingenuity from scientists at NIH and Amgen to convert this invention into a clinical application.

Amgen, a company working in the field of chemotherapy, approached NIH for licensing the technology. Knowing that Amgen had worked with other growth factors such as PDGF and G-CSF and that KGF would fit well in its portfolio, NIH granted them an exclusive license in 1992. Once the license agreement was made, both NIH and Amgen scientists committed themselves to overcome the difficulties in the clinical development path of KGF. While there were many technical challenges, there were also eureka moments and turning points that foreshadowed the development of KGF as a significant advance in cancer therapy. In December 2004, the FDA approved KGF/palifermin for reduction of the incidence and duration of severe oral mucositis in patients with hematological cancers undergoing bone marrow/ blood cell transplantation[1]. Amgen markets this drug under the trade name of Kepivance™[4]. The use of Kepivance™ may significantly reduce medical costs through the prevention or reduction of oral mucositis in this patient population. Kepivance™ may also enable patients to undergo full doses of treatment, acquire fewer infections, and/or reduce their time in the hospital.

Dr. Rubin, the lead inventor whose science has enriched the lives of cancer patients, hopes that KGF will establish a place for itself in the cancer armamentarium. He also hopes that KGF finds a clinical use in many of the other settings where it is being tested. These include solid cancers, such as colorectal, head and neck, and lung, where substantial radiation damage to the oral cavity takes place. More than any other benefit, as improved treatments transform cancer from an acute life-threatening disease to a chronic disease, agents like KGF pave the way for new drugs that will allow patients to enjoy a better quality of life during their remaining years.

References

1. Garfunkel AA, “Oral mucositis - the search for a solution”, *NEJM*. 2004; 351:2649-2651.
2. Spielberger R, Stiff P, Bensinger W, et al. “Palifermin for oral mucositis after intensive therapy for hematologic malignancies”, *New England Journal of Medicine*. 2004; 351:1590-1598.
3. Rubin JS et al “Purification and characterization of a newly identified growth factor specific for epithelial cells” Proc. Natl. Acad Sci USA 1989; 86(3): 802-806.
4. Amgen press release December 15, 2004. “FDA Approves Kepivance for Severe Oral Mucositis in Cancer Patients Undergoing Bone Marrow Transplant; Pivotal Phase 3 Study Published in This Week's *New England Journal of Medicine*”.

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