Discussion

Wound healing is a complex and coordinated process beginning with tissue injury [2–4]. After tissue injury, a coagulation cascade is activated to stop bleeding. Inflammatory mediators are then activated, resulting in an outpouring of cytokines and growth factors that initiate collagen repair and granulation tissue formation. The final process, which completes the healing process, involves extracellular tissue remodeling, angiogenesis and reproduction of the original tissue.

Keratinocytes play a key role in skin healing in response to injury. Keratinocytes not only proliferate to complete tissue healing, but they also serve as a source of several cytokines. EGFR ligands are among the most prominent cytokines secreted by the keratinocytes [2]. EGFR ligands include epidermal growth factor (EGF), transforming growth factor-α, amphiregulin, heparin binding EGF-like growth factor (HB-EGF), betacellulin and epiroregulin [5]. These secreted cytokines stimulate adjacent keratinocytes. There appears to be a biphasic production of EGFR ligands during the wound healing process. The first phase of production of EGFR ligands is secondary to local induction in response to injury; the second wave of production is secondary to autocrine activation of the keratinocytes. Some evidence suggests that HB-EGF is the most important of the ligands. The activation of EGFR and vascular endothelial growth factor receptor promotes wound healing. Consequently, agents that inhibit EGFR could potentially interfere with wound healing. Topical application of OSU 8-1, an inhibitor of EGFR ligand shedding, has been shown to decrease keratinocyte migration and delay cutaneous wound healing [3]. In addition, systemic administration of gefitinib has been shown to decrease epithelial proliferation and stratification in response to corneal injury [5].

Gefitinib is absorbed orally and inhibits skin EGFR phosphorylation. Gefitinib accumulates in the skin, which means theoretically that patients treated with this agent could have problems with wound healing. Preclinical studies have shown that gefitinib can delay and inhibit corneal wound healing [5]. Gefitinib has not been shown to impair skin wound healing in our small series reported here. This data suggests that the role of EGFR in wound healing needs to be re-evaluated.

Disclosure

R. G. has received honoraria from Astra Zeneca for speaking engagements.

R. Govindan1,2*, D. Behnken1,2, W. Read1,2 & H. McLeod1,2

1Washington University School of Medicine, St Louis, MO; 2Alvin J Siteman Cancer Center, St Louis, MO, USA (*E-mail: rgovinda@im.wustl.edu)

References


DOI: 10.1093/annonc/mdg352

Radiotherapy following breast-conserving surgery

I read Chung and Cady’s letter urging caution with repeat sentinel node biopsy [1] with some alarm. Surely the other pertinent point that this case illustrates is the imperative to irradiate the breast following breast-conserving surgery, a procedure now accepted as standard, to reduce local recurrence in the remaining breast tissue [2]. The patient reported in this case did not receive radiotherapy to the breast following wide local excision, despite this being a standard procedure, and 20 months after diagnosis she presented with local recurrence. As the authors themselves state, local recurrence is an indication that the patient is at risk of systemic disease [3, 4], and indeed 10 months later, this 48-year-old patient with a T1a tumour presented with lung and liver metastases. This is clearly a very poor outcome for all concerned. Whilst the role of radiotherapy following mastectomy for histologically high-grade but node-negative breast cancer remains controversial, its use following breast-conserving surgery, even in seemingly low-risk women such as the patient described, is clear, and this unfortunate case clearly illustrates this point.

A. L. Appleton

Unité de Sénologie, Clinique de Genolier, near Geneva, Switzerland, CH-1272 (E-mail: appleton@cdg.ch)

References


DOI: 10.1093/annonc/mdg355