Top Stories in Research

By Dr. Jan Dutz

What's new on the research front? The articles from which these summaries of the latest in skin research are taken are so hot off the press the ink has barely dried.

Molecular profiling to treat melanoma

Catching melanoma early, before it has spread from the skin, is important. Once malignant melanoma has metastasized, or spread past the skin, the outlook for long-term survival is poor. For example, the survival of patients with melanoma that has spread to internal organs such as the lungs or liver is in the order of just eight to 18 months. Unfortunately, melanoma cells—derived from melanocytes, or pigment cells—are exceptionally hardy and are not destroyed by common chemotherapy regimens.

Melanomas arise when mutations occur in the genetic material of melanocytes. Mutations in the *BRAF* gene, which controls signalling within the cell, are found in up to 50 per cent of patients with metastatic disease. A pharmaceutical company has recently developed an inhibitor of *BRAF*. In a study published in the *New England Journal of Medicine*, patients with metastatic melanoma were tested for the genetic mutation in *BRAF*. Patients with this mutation were then randomly treated with either a *BRAF* inhibitor called vemurafenib or standard chemotherapy. In this study, treatment of patients with a *BRAF* mutation with vemurafenib resulted in a 63 per cent reduction in risk of death when compared with standard therapy.

This paper demonstrates that molecular profiling (identifying specific mutations) of cancer cells and mutation-directed treatment can result in better outcomes for patients.

Molecular profiling to prevent drug eruptions

Skin rashes are a relatively common side effect of systemic drug therapy and they account for most of the adverse reactions to drugs in hospitalized patients. Skin rashes generally occur weeks after the responsible drug is first taken, but may recur rapidly when the drug is taken for a second or third time. Skin rashes caused by drugs are often uncomfortable and itchy but resolve over one or two weeks when the drug is discontinued.

Stevens–Johnson syndrome, and a severe form called toxic epidermal necrolysis, is a rare but particularly severe form of drug eruption that can be life-threatening. In this condition, the skin is damaged by an overactive immune system. This results in skin death and extensive peeling, often involving the mouth and eyes.

Three recent studies—two published in the *New England Journal of Medicine* and one in *Human and Molecular Genetics*—have examined molecular markers that may predict such a severe drug eruption in response to specific drugs and in specific populations. These studies have shown that specific tissue-type molecules (termed HLA-A and HLA-B) are associated with this severe drug reaction in response to exposure to the anti-seizure medicine carbamazepine. One study found that the frequency of this reaction could be significantly decreased if people of Han Chinese descent with a specific HLA-B molecule avoided the drug. Another study linked the severe reaction to HLA-A in people from Japan and northern Europe. These studies suggest that specific ethnic groups are particularly at risk of certain drug eruptions and that screening can identify patients at risk of severe adverse reactions to specific drugs.

These are two examples of the genetic and molecular characterization of patients and patient material. The result is what is known as "personalized medicine," with improved outcomes.

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