Nature Reviews Cancer | AOP, published online 30 April 2009; doi:10.1038/nrc2661

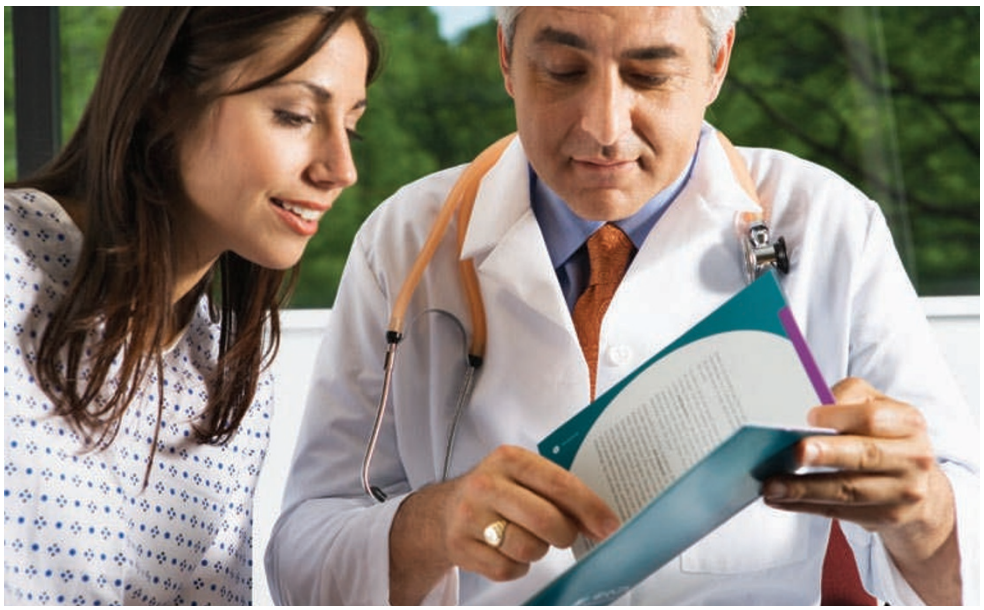
MELANOMA

A more accurate diagnosis

Melanoma is one of the most common types of cancer, but histopathological diagnosis of malignant melanoma versus atypical benign naevi can be difficult as many of the diagnostic criteria overlap. The design of a novel multi-marker assay that can distinguish between melanoma and benign naevi is therefore an important advance.

Building on a previous study in which they showed that naevi and melanomas have distinct gene expression profiles, Mohammed Kashani-Sabet and colleagues selected five of these differentially expressed genes for the development of a diagnostic assay. They selected these markers (ARPC2, FN1, RGS1, SPP1 and WNT2) on the basis of statistically significant differences in expression in clinical naevi and melanoma samples, as well as the commercial availability of antibodies. Using immunohistochemistry, they analysed the expression of the markers in a training set of 534 samples of melanomas and naevi. Each of the markers was significantly overexpressed in melanomas compared with naevi. Moreover, the pattern of antibody staining was different in melanomas and benign naevi, with the benign naevi showing higher marker expression at the junctional zone than at the base, whereas the staining in melanomas was more homogenous.

CORBIS



Kashani-Sabet *et al.* used the differences that they had detected in marker expression to develop a diagnostic algorithm that incorporated the five markers. They then tested this algorithm in four validation sets comprising melanoma that arose in a naevus, dysplastic naevi, Spitz naevi and previously misdiagnosed melanocytic neoplasms. Their assay diagnosed melanomas that arose within a naevus with 95% specificity and 97% sensitivity, and also correctly diagnosed 75% of samples that were previously misdiagnosed using other methods. The authors found that more than one marker is necessary to accurately diagnose melanoma samples: although WNT2 was the best single marker in the training set, including the other four markers was important for the high level of diagnostic accuracy of the test.

Many of the markers incorporated into this new assay have been previously implicated in tumorigenesis; for example, WNT2 is important for melanoma cell proliferation. Therefore, in addition to their use as diagnostic markers, these biomarkers may also have a direct role in promoting melanoma progression.

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ORIGINAL RESEARCH PAPER Kashani-Sabet, M. *et al.* A multi-marker assay to distinguish malignant melanomas from benign nevi. *Proc. Natl Acad. Sci. USA* 30 Mar 2009 (doi: 10.1073/pnas.0901185106)