A fit of activity has permeated the melanoma research and treatment front in recent years. Several new drugs have been approved, and many others are in development. Meanwhile, new publications continue to elucidate the significance of new pathways and genomic factors. Many of these developments can be categorized as part of one of the most compelling and certainly significant periods of research in the melanoma spectrum: It’s being termed as the dawn of the “molecular” era in melanoma treatment.

Earlier this year, an article published in *The British Journal of Dermatology* noted that “melanoma is leading the field of cancer research in the molecular approach to therapy of advanced disease.” Reviewing recent progress in the development of novel molecular markers for melanoma that are nearing clinical application, the author took stock of the latest developments in the molecular classification, diagnosis, and assessment of melanoma, suggesting that the molecular era of melanoma may result in significant shifts in understanding and treating melanoma.

**THE SIGNIFICANCE OF MOLECULAR MARKERS**

Molecular markers will have major relevance in melanoma research and treatment. We have already seen how molecular markers help define treatments. For instance, in an article published in *The New England Journal of Medicine* just last month, the combination dabrafenib-trametinib (Tafinlar plus Mekinist, GlaxoSmithKline) was found to improve the rate of progression-free survival in previously untreated patients who had metastatic melanoma with BRAF V600E or V600K mutations.

Molecular understanding is also bringing about significant change in the way we consider melanoma. Recently three major new genes have been identified that expand our awareness of the melanoma growth cycle. We are moving from phenotype to genotype in identifying high-risk individuals. This will ultimately lead to therapeutic changes.

The new major genes identified include TERT, BAP1, and MITF:

**Telomerase Reverse Transcriptase** (TERT) maintains caps at chromosomal ends to ensure the cell life cycle. When TERT is decreased, there is chromosomal instability and cell death. There appears to be a variety of telomerase upregulating changes in melanoma cell lines. This can also be seen in other cancers.

**BRCA1 Associated Protein-1** (BAP1) is a gene leading to tagging of individual proteins destined for destruction. If BAP1 does not function there may be destruction of growth inhibiting proteins and insufficient removal of growth promoting proteins.

Finally **Microphthalmia Associated Transcription Factor** (MITF) may be the ultimate regulator over melanoma growth—it’s inability to control cell division may be the connecting factor between all these pathways.

**CHANGING EVERYTHING**

When it comes to the role of genetics in the classification, diagnosis, and treatment of melanoma, more knowledge has been gained over the past 24 to 48 months than ever before. And although we are just beginning to understand the role of genetics in melanoma, we are already seeing the impact of having reached a new plateau in melanoma care through earlier diagnosis, understanding of high-risk lesions, risk stratification, and prognostics models. In short, the molecular era of melanoma is likely to change everything.

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