Preface

## Focused issue on "Melanoma"

This focused issue of *Annals of Translational Medicine* reviews the state of the art in melanoma. Experts in the field review the most relevant findings about biology, genetics and new treatments for melanoma.

As the Guest Editor of this issue, I would try to provide simple keys of lecture that might help illustrate the conceptual basis and at least some of the potential future developments for melanoma management.

This issue includes a review from Dr. Potrony about familial melanoma. Dr. Potrony, on Dr Puig's team in Barcelona, is an expert on hereditary melanoma and her group has become one of the essential references in this field. In this paper, she outlines the most important genes involved in familial melanoma and helps us understand the molecular biology of the disease.

Other articles about melanoma genetics are included in this issue. One of them is by Dr. Karachaliou, who reviews the most relevant aspects on molecular signalling in melanoma pathogenesis and evolution, with a special focus on translational research. The other one is a review by Dr. Martinez-Cardus, on Dr. Esteller's team, who reviews the epigenetic alterations that regulate molecular patterns of melanoma and their possible role as a resistant mechanism to chemotherapy. Dr. Molina reviews data on liquid biopsies in cancer, especially in melanoma. Liquid biopsies are now a promising tool for diagnosis and follow up, and could provide prognostic information. Our team has developed its own methodology based on a modified PCR technique that can be easily applied in the clinical setting.

This focused issue also deals with new treatments and the clinical management of melanoma. Dr. Cortes and Dr. Muñoz from Hospital Vall D'Hebron in Barcelona have reviewed the clinical data of BRAF and MEK inhibitors in melanoma, while Dr. Manzano reviews the different resistant mechanisms that have been described until now, to help us understand how they might be overcome. A third paper on therapy includes a review on new target drugs that could be active in melanoma, attending to preclinical or early clinical trials data. From the Spanish Melanoma Group (GEM), my colleagues Dr. Algarra, Dr. Berrocal, Dr. Soria, Dr. Pantic and Dr. Cerezuela have written an update of clinical results with immunotherapy, focused on anti PD-1 and anti CTLA-4 drugs. Dr. Teixido completes this section with a review on predictive markers of response to anti PD-1/PD-L1 inhibitors.

For decades there were no advances in treatment for metastatic melanoma, although old immunotherapy modalities, such as high doses of IL-2 or cellular vaccines, demonstrated activity in some individual cases, median survival of metastatic melanoma patients did not improve. In recent years this situation has changed dramatically. Several active treatments for melanoma have been approved and now melanoma is a model for the development of treatment for other tumors. Drugs such as BRAF and MEK inhibitors obtain a clear survival advantage with high response rates. Immunotherapy with anti CTLA-4 antibody (ipilimumab) and the anti PD-1/PD-L1 inhibitors (nivolumab and pembrolizumab) has demonstrated activity with long lasting responses.

With this focused issue, we attempt to offer the most relevant and up-to-date information on this dynamic field, in the hope that it is helpful for clinical oncologists and other specialists involved in the care of melanoma patients.

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