**The importance of partial losses of chromosome 3 in uveal melanoma in the region encompassing the BAP1 gene**

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Close to 30 years ago, three research groups independently described chromosomal abnormalities in primary uveal melanoma, with all three highlighting the presence of monosomy 3 in some of the examined cases. All groups proposed that monosomy 3 may play an important role in uveal melanoma progression. This was later confirmed by Prescher and co-workers, who examined the outcome of 54 primary uveal melanoma patients, 30 (55%) of whom had monosomy 3 tumours, and with 17 of these 30 patients (57%) succumbing to their disease within 3 years (1). In the meantime, numerous research groups have confirmed the significance of monosomy 3 loss in primary uveal melanoma; while the Liverpool Ocular Oncology Clinic translated this fundamental science into clinical care. Damato et al. used cytogenetic testing of consented primary uveal melanoma patients to stratify them into risk groups with respect to metastasis development, and to determine liver surveillance management (2). In the meantime, molecular genetic testing has been incorporated into algorithms integrating other known strong prognostic parameters, in order to refine metastatic risk prediction in uveal melanoma patients (3). Over the last decade, our understanding of the underlying mutations present in primary uveal melanoma and how these may link to the described chromosomal alterations has advanced significantly (4). Of particular importance is the gene *BAP1* (3p21.31-p21.2), and its temporal and functional association with the loss of one copy of chromosome 3.

Rodrigues and co-workers in the current paper examined retrospectively 1088 uveal melanomas, which had been examined using comparative genomic hybridization arrays. They established that 4% of these tumours were characterised by partial loss of chromosome 3. This frequency is similar to that documented in some previous studies, but the significance of this finding is controversial because of considerable variability in reported mortality rates of affected patients (5). The differing methodologies applied as well as different classification criteria used, make it difficult to compare these studies. In the current paper, however, Rodrigues and coworkers go further in their analysis and examine the relationship of the partial chromosome 3 loss with its involvement with the BAP1 gene. They have been able to convincingly demonstrate that the partial loss of chromosome 3, which encompasses the *BAP1* locus, is associated with a poorer outcome. This interesting finding emphasises the importance of *BAP1* alterations as the driver of metastatic risk in uveal melanoma cases with either complete or partial loss of one copy of chromosome 3. Indeed, we have reported that monosomy 3 cases without BAP1 alterations show prolonged survival (6). Of increasing importance, therefore, are new technologies, such as next generation sequencing, which can allow for the simultaneous and targeted analysis of both copy number variation and mutations, as has already been done for uveal melanoma (7). The flexibility of this technology allows for the incorporation of additional genes, should more be revealed to be of prognostic relevance.

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