Cancer-associated SF3B1 mutations affect alternative splicing by promoting alternative branchpoint usage.

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**Résumé**

Hotspot mutations in the spliceosome gene SF3B1 are reported in ~20% of uveal melanomas. SF3B1 is involved in 3′-splice site (3′ss) recognition during RNA splicing; however, the molecular mechanisms of its mutation have remained unclear. Here we show, using RNA-Seq analyses of uveal melanoma, that the SF3B1(R625/K666) mutation results in deregulated splicing at a subset of junctions, mostly by the use of alternative 3′ss. Modelling the differential junctions in SF3B1(WT) and SF3B1(R625/K666) cell lines demonstrates that the deregulated splice pattern strictly depends on SF3B1 status and on the 3′ss-sequence context. SF3B1(WT) knockdown or overexpression do not reproduce the SF3B1(R625/K666) splice pattern, qualifying SF3B1(R625/K666) as change-of-function mutants. Mutagenesis of predicted branchpoints reveals that the SF3B1(R625/K666)-promoted splice pattern is a direct result of alternative branchpoint usage. Altogether, this study provides a better understanding of the mechanisms underlying splicing alterations induced by mutant SF3B1 in cancer, and reveals a role for alternative branchpoints in disease.

**Résumé**

Hormone receptor status and HER2 status are of critical interest in determining the prognosis of breast cancer patients. Their status is routinely assessed by immunohistochemistry (IHC). However, it is subject to intra-laboratory and inter-laboratory variability. The aim of our study was to compare the estrogen receptor, progesterone receptor and HER2 status as determined by the MapQuant™ test to the routine immunohistochemical tests in early stage invasive breast cancer in a large comprehensive cancer center.

**Massively parallel DNA sequencing from routinely processed cytological smears.**
*Cancer cytopathology*: 241-53 : [DOI: 10.1002/cncy.21639](http://dx.doi.org/10.1002/cncy.21639)

**Résumé**

Data generated by next-generation sequencing technologies have a pivotal role in precision medicine. These high-throughput techniques are preferentially performed on fresh tissue, but there is an increasing need for protocols adapted to materials derived from formalin-fixed, paraffin-embedded tissue and cytology specimens.

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**Balanced Translocations Disrupting SMARCB1 Are Hallmark Recurrent Genetic Alterations in Renal Medullary Carcinomas.**
*European urology*: [DOI: S0302-2838(15)00935-5](http://dx.doi.org/10.1016/j.eururo.2015.08.005)

**Résumé**

Renal medullary carcinoma (RMC) is a rare and highly aggressive neoplasm that most often occurs in the setting of sickle cell trait or sickle cell disease (SCD). Most patients present with metastatic disease resistant to conventional chemotherapy, and therefore there is an urgent need for molecular insight to propose new therapies.