# *NAB2-STAT6* **fusion** (Non-core)

**Reason/Evidentiary Support**

In-frame *NAB2-STAT6* gene fusions result from chromosome 12q13 inversions and represent highly sensitive and specific signature alterations of meningeal solitary fibrous tumour/haemangiopericytoma (SFT/HPC) of grade 1, 2, or 3; these fusions are also characteristic of the analogous soft tissue/extracranial counterparts, which are referred to as SFT or malignant SFT. Given the relative ease of detecting this genetic alteration using a STAT6 immunohistochemical surrogate (see **STAT6 expression (immunohistochemistry)**), diagnostic confirmation is highly recommended in the WHO 2016 classification scheme before a diagnosis of SFT/HPC is rendered.[1,2]

*NAB2-STAT6* Gene Fusion

*NAB2-STAT6* gene fusions are detectable using RT-PCR or various other sequencing techniques, including NGS if designed appropriately.[3,4] Over 40 fusion variants have been detected to date, with the most common meningeal SFT/HPC subtypes fusing exon 6 of *NAB2* with exons 16, 17, or 18 of *STAT6* (roughly one-half of all cases).[4] Preliminary data also suggests that the *NAB2* exon 4-*STAT6* exon 2/3 fusions are more common in the lower grade and clinically less aggressive SFT/HPC, though larger studies are needed for further validation.[4,5]

STAT6 Nuclear Expression (Immunohistochemistry)

The STAT6 protein is normally expressed in the cytoplasm of cells, whereas NAB2 is expressed in nuclei; however, the *NAB2-STAT6* fusions cause the STAT6 protein to translocate to the nucleus. As such, STAT6 immunohistochemistry represents a highly reliable and practical surrogate for detecting this signature alteration, with nearly 100% sensitivity and specificity regardless of the fusion variant.[3,6] Nearly all meningeal SFT/HPC and extracranial SFTs display strong and extensive/diffuse nuclear positivity, whereas other diagnostic considerations, such as meningiomas, nerve sheath tumours, and various sarcomas, either lack expression or show only cytoplasmic staining. As such, the pathologist is cautioned against rendering a diagnosis of SFT/HPC in the absence of nuclear STAT6 immunoreactivity.

**References**


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