NEURO-ONCOLOGY

FSTL5—a new prognostic biomarker for medulloblastoma

Expression levels of the protein follistatin-like 5 (FSTL5) indicate poor prognosis in subtypes of medulloblastoma that are poorly characterized, a new study has shown.

Medulloblastoma is the most common malignant brain tumor in pediatric patients. Disease outcome can vary considerably from patient to patient despite similar clinical features, thereby hampering clinical trials and effective treatment.

Tumorigenesis driven by aberrant activity of the WNT pathway or of sonic hedgehog (SHH) signaling constitute two variants of medulloblastoma. The other two variants identified have been designated type C and type D tumors. “The underlying biology of non-WNT/SHH tumors remains poorly understood, and the prognosis of these subgroups was generally thought to be particularly unfavorable,” says Stefan Pfister, who is at the University of Heidelberg, Germany, and was involved in the study.

The researchers began by performing a genome-wide transcriptome analysis of 64 primary medulloblastoma samples from a cohort of patients with detailed

follow-up data. The results highlighted increased *FSTL5* expression as a novel marker of poor prognosis.

“...FSTL5 immunoreactivity showed a significant inverse correlation with survival”

Importantly, low expression of *FSTL5* was associated with good prognosis even in patients with non-WNT/SHH tumors. “Addition of this single complementary marker may prove useful in delineating patients in the intermediate–high-risk group who would benefit from current treatment strategies and show a similar prognosis to WNT and SHH subgroups,” explains Pfister. “Future clinical trial design should take transcriptomic subgroups into account, because of the important clinical differences—demographics, metastatic potential, and response to treatment,” he adds.

Next, the team investigated *FSTL5* protein expression by means of immunohistochemistry in 235 medulloblastoma samples. Similar to the genetic findings, *FSTL5* immunoreactivity showed a significant inverse correlation

with survival. “The readout is particularly useful as immunohistochemistry is widely used in neuropathological laboratories and easy to evaluate,” says Pfister.

Differential expression of markers between adult and pediatric patients has been shown previously. However, further analysis by Pfister and colleagues revealed that *FSTL5* expression predicts prognosis independently of age, underscoring the broad applicability of this marker in various patient subgroups.

Together, these results identify *FSTL5* as a readily accessible and specific marker of poor prognosis that could be incorporated into existing molecular profiling schemes to improve patient stratification.

“The role of *FSTL5* in medulloblastoma tumorigenesis remains poorly understood,” says Pfister. “It will be interesting to see whether this marker has any biological importance.”

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