

# 6<sup>th</sup> Munich Biomarker Conference

Clinical Practice and Targeted Therapies in Personalized Medicine

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## Conference Guide



## Key Wnt signalling molecules as potential biomarkers of astrocytic brain tumors

### Abstract

#### Introduction

Wnt pathway has been established as one of the basic signalling pathways whose misregulation often governs tumorigenesis. Astrocytic brain tumors are classified according to their lineage of origin and behavior into four WHO grades. In spite of recent progress on the elucidation of astrocytoma genetics, molecular mechanisms responsible for their formation and progression are still inadequately explained. In the present study key players of the Wnt signalling: beta-catenin (CTNNB1), TCF1, LEF1, SFRP3 and Dishevelled-1 (DVL1) were investigated.

#### Materials and methods

Gene changes were tested by polymerase chain reaction/loss of heterozygosity (LOH) using MSI analysis, and proteins expressions by immunohistochemistry, digital scanning and image analysis.

#### Results and discussion

Our results demonstrated that 50% of glioblastomas (grade IV) and 56% of astrocytomas (grades II and III) showed upregulation of beta-catenin. Its nuclear localization which is an indicator of pathway's activation was found in 52.1% of glioblastomas. Furthermore, transcription factors of the pathway were upregulated, too. Strong TCF1 and LEF1 expression was observed in 51.6% and 71% of gli-

blastomas. Astrocytomas grade I showed weak or no expression in the 63.2% for TCF1 and 68.2% for LEF1. The F-ratios for two variables (LEF1 strong and LEF1 weak) indicated that differences between astrocytomas (II, III) and glioblastomas were statistically significant ( $p < 0.02$ ). Discriminant function analysis further showed that just one variable – the strong expression of LEF1, emerged to discriminate between astrocytomas and glioblastomas. This suggests that LEF1 may serve as a potential diagnostic marker. Dishevelled 1 was also targeted in glioblastoma showing 9.4% LOH and 21.9% MSI. We have also demonstrated that moderate ( $P = 0.002$ ) and strong ( $P = 0.018$ ) SFRP3's nuclear expression decreased in higher grade astrocytomas in comparison to low grade. Whereas, when located in the cytoplasm an increased expression of SFRP3 was identified in the high grade astrocytomas ( $P = 0.048$ ). This may suggest that SFRP3 can also act as an agonist of Wnt signaling and promote invasive behavior.

#### Conclusion

Our findings contribute to better understanding of human astrocytic brain tumor genetic profile and suggest that Wnt signalling plays important role in its etiology. The findings may provide molecular biomarkers that will help in diagnostics and therapeutic decision-making.

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