

Epigenetics of paediatric glioma stem cells; focusing on exosomes, miRNAs and DNA methylation

Akademisk avhandling

som för avläggande av medicine doktorexamen vid Sahlgrenska akademien,
Göteborgs universitet kommer att offentligens försvaras i Arvid Carlsson Hörsal,
Academicum, Medicinaregatan 3,
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av **Ágota Túzesi**

Fakultetsopponent:

Professor Mattias Belting
Lund University, Sweden

Avhandlingen baseras på följande delarbeten:

- I. **Túzesi Á**, Kling T, Wenger A, Lunavat TR, Jang SC, Rydenhag B, Lötvall J, Pollard SM, Danielsson A and Carén H.; Pediatric brain tumor cells release exosomes with a miRNA repertoire that differs from exosomes secreted by normal cells. *Oncotarget*, 2017 Oct 6;8(52):90164-90175.
- II. **Túzesi Á**, Wenger A, Magnusson M, Danielsson A, Kling T and Carén H. The role of miR-497-5p in mediating response to temozolomide in paediatric glioma stem cells. *Manuscript in preparation*.

**SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR BIOMEDICINE**



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Abstract

Tumours in the central nervous system are accountable for the majority of cancer-related deaths in children. Glioblastoma multiforme, one of the deadliest of the central nervous system tumours, is partly driven by glioma stem cells. The generation and maintenance of these cells is orchestrated by complex genetic and epigenetic mechanisms.

This thesis investigates the role of two epigenetic players, miRNAs and DNA methylation, as well as the involvement of exosomes in paediatric glioma stem cells. The first study profiles the miRNA content of these cells and compares it to normal neural stem cells. Furthermore, the miRNA content of the exosomes secreted by glioma stem cells and its effect on normal stem cells is determined. The second study investigates how specific miRNAs are regulated and how they could potentially influence glioma stem cells' response to the chemotherapeutic agent temozolomide.

These studies provide new insights into the multifaceted epigenetic regulation of glioma stem cells. The gained knowledge could lead to a better understanding of the biological processes behind brain tumours.

Keywords: epigenetics, microRNA, DNA methylation, exosomes, glioblastoma, paediatric, glioma stem cells, neural stem cells, TMZ response.