GLYCAN MEDIATED FUNCTION OF OSTEOPONTIN

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Osteopontin (OSTP) is a highly phosphorylated and glycosylated extracellular matrix protein that plays a pivotal role in bone remodeling and wound healing, also in inflammation and tumor progression [1]. The specific glycosylation pattern of OSTP tips the balance of those processes through interactions with glycan-binding proteins [2]. Yet, the precise regulation mechanism remains not fully understood at molecular level.
We herein present a synergic combination of NMR and LC-MS/MS to precisely characterize the glycoprofile of OSTP, recombinantly produced in HEK293 cells [3]. State-of-the-art NMR binding experiments revealed, at atomic resolution, the glycan mediated interactions between OSTP and key members of the glycan-binding protein family of Galectins, known to play a role in cancer progression. These findings offer new insights into the structural basis of OSTP's elusive glycan recognition mode and its regulatory role in biochemical processes.
We have further explored the interaction of OSTP with the CD44 receptor, which is involved in the activation of the PI3K/AKT signaling pathway in non-small cell lung carcinoma and promotes tumor cell migration. We have finally examined the interplay with Galectin-8 (Gal8), a known binding partner of CD44 [4].
Our structural insights have been validated *in cellulo* by biological assays, demonstrating the formation of the OSTP/CD44/Gal8 ternary complex and its effects on downstream signaling events, including cell apoptosis and survival pathways.
Our findings pave the way to illuminate previously uncharted glycan-mediated interactions, advancing the structural and functional understanding of OSTP's role in cancer biology and paving the way for potential therapeutic interventions targeting glycan recognition pathways.

References:
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