

New challenges in anticoagulation therapy: Protein S

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Protein S is a vitamin-K dependent anticoagulant plasma glycoprotein; its main function being a cofactor for Protein C in the inactivation and degradation of coagulation factors Va and VIIIa. As an anticoagulant, Protein S also binds directly to coagulation factors Va and VIIIa, in an aPC-independent manner, thus possessing a direct anticoagulant activity.

Deficiency or impaired bioactivity of Protein S leads to life threatening pro-thrombotic conditions and is a risk factor for Deep Vein Thrombosis (DVT). As a vitamin-K dependent protein, its bioactivity is compromised following systemic anticoagulant treatment with vitamin K inhibitors such as Coumadin/Warfarin. Protein S is a multifunctional protein, with important roles outside the coagulation system. Most prominently, Protein S is a ligand for the proto-oncogenic TAM subfamily of tyrosine kinase receptors comprising of Tyro3, Axl and Mer. Regulated signaling through TAM receptors is necessary for homeostatic regulation of various adult systems, including the immune, vascular, nervous and reproductive systems. Additionally, Protein S plays a prominent role in clearance of apoptotic cells. Studying the roles of Protein S outside the coagulation system, we generated a conditional knockout mouse model targeting the PROS1 gene. Using this mouse model, we identify new roles for Protein S in the nervous system and vasculature, thus pointing to its importance in several physiological niches. Revealing additional roles for Protein S highlights its importance in multiple systems, and suggests a mechanistic understanding of potential physiological effects and consequences following anticoagulation treatment based on vitamin-K inhibitors.

Biography

Tal Burstyn-Cohen has completed her Ph.D. from The Hebrew University of Jerusalem, and pursued two postdoctoral studies, one from The Hebrew University of Jerusalem and another from The Salk Institute for Biological Studies, La Jolla. With a strong background in developmental neurobiology, she now studies the physiological roles of Protein S and the TAM receptors. She heads a research group as the Principal Investigator. She has published more than 15 papers in reputed journals.

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