Serglycin – implications in granulogenesis of neutrophils

Carsten Utoft Niemann

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Official opponents: Ole W. Petersen, Peter Hokland and Svein O. Kolset, Norway.

Tutors: Niels Borregaard.

Correspondence: Carsten U. Niemann, Magledalen 17, 2860 Søborg, Denmark.

E-mail: niemann@dadlnet.dk

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ABSTRACT

The dissertation is based on experimental work performed in The Granulocyte Research Laboratory, Department of Haematology, H:S Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark in the period 2003-2006. It consists of four studies.

The aim of the study was to investigate the expression, localization, and function of serglycin proteoglycan in neutrophils. Serglycin is an intracellular proteoglycan with a core protein of 17.6 kDa and glycosaminoglycan side chains of more than 200 kDa. A function of serglycin in granule formation, in targeting of proteins to granules, and in packaging granule proteins has been proposed.

Serglycin proteoglycan was localized to the Golgi stacks and immature granules in promyelocytes and myelocytes (progenitors of neutrophils) from human bone marrow. Serglycin was absent from mature neutrophils and granule proteins were shown not to be packaged as macromolecular complexes.

By means of a serglycin knock-out mouse model, neutrophil elastase was shown to be dependent on serglycin for localization in azurophil granules of neutrophils. The lack of serglycin, and thereby lack of neutrophil elastase, compromised the in vivo bactericidal activity of neutrophils against Gram-negative *Klebsiella pnuemoniae.*

The expression of serglycin was characterized for different haematological malignancies. Serglycin was proposed as a marker of immature myeloid cells.

The previously proposed role of serglycin in localizing zymogens of exocrine pancreas to zymogen granules in pancreatic acinar cells was investigated. It was clarified that serglycin is neither expressed in human nor murine pancreas. The localization of zymogens is unaffected by the lack of serglycin in a serglycin knock-out mouse model.

Together these data characterize a function for serglycin during myelopoiesis that is specific for neutrophil differentiation. Analogous functions have been characterized in other haematopoietic cells.