
Polysialic acid governs T-cell development by regulating progenitor access to the thymus.

Journal: Proc Natl Acad Sci U S A

Publication Year: 2009

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PubMed link: 19587240

Funding Grants: Profiling surface glycans and glycoprotein expression of human embryonic stem cells , Human Stem Cell Training at UC Berkeley and Childrens Hospital of Oakland

Public Summary:

Scientific Abstract:

Although the polysialyltransferase ST8Sia IV is expressed in both primary and secondary human lymphoid organs, its product, polysialic acid (polySia), has been largely overlooked by immunologists. In contrast, polySia expression and function in the nervous system has been well characterized. In this context, polySia modulates cellular adhesion, migration, cytokine response, and contact-dependent differentiation. Provocatively, these same processes are vital components of immune development and function. We previously established that mouse multipotent hematopoietic progenitors use ST8Sia IV to express polySia on their cell surfaces. Here, we demonstrate that, relative to wild-type controls, ST8Sia IV(-/-) mice have a 30% reduction in total thymocytes and a concomitant deficiency in the earliest thymocyte precursors. T-cell progenitors originate in the bone marrow and are mobilized to the blood at regular intervals by unknown signals. We performed in vivo reconstitution experiments in which ST8Sia IV(-/-) progenitors competed with wild-type cells to repopulate depleted or deficient immune subsets. Progenitors lacking polySi exhibited a specific defect in T-cell development because of an inability to access the thymus. This phenotype probably reflects a decreased capacity of the ST8Sia IV(-/-) progenitors to escape from the bone marrow niche. Collectively, these results provide evidence that polySia is involved in hematopoietic development.

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