PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

T cell homeostasis in patients with rheumatoid arthritis

ArticleInfo		
ArticleID	:	129
ArticleDOI	:	10.1186/ar-2000-66867
ArticleCitationID	:	66867
ArticleSequenceNumber	:	86
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2000–12–4 OnlineDate : 2000–12–4
ArticleCopyright	:	Current Science Ltd2000
ArticleGrants	:	
ArticleContext	:	130753311

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Keywords

CD45, RA, T-cell differentiation, telomere, thymus, TREC

Context

Immune abnormalities have been documented in rheumatoid arthritis (RA) patients and are reminiscent of those seen in an aged immune system. Defects observed in the naive-T-cell compartment have raised the possibility of a defect in thymic function, which in turn will impose a proliferative stress on the total-T-cell compartment. In this paper, the authors address the issue of naive-T-cell homeostasis by determining the level of T cells that have T-cell receptor excision circles (TRECs), alongside telomere length and proliferative capacity, in RA patients compared to age-matched controls.

Significant findings

TRECs were reduced in RA peripheral blood, independent of disease duration. $CD4^+$ and $CD8^+$T cell telomere lengths were also reduced. This reduction was most marked in CD45ROnull cells, which display a lower proliferative potential compared to age-matched controls. The authors suggest that there is either a primary defect in T-cell generation, an increased T-cell turnover or a mixture of both. A normal naive : memory ratio in RA patients reduces the likelihood of an antigen-dependent T-cell expansion and reinforces the possibility of naive T cell proliferation to compensate for poor thymic function.

Comments

This work sheds light on the critical problem of tuning the balance between T-cell generation, T-cell death and T-cell replication in RA. TRECs reflect dynamic processes, and cannot differentiate between altered entry into or exit from the peripheral T-cell pool. Because the abnormalities were detected at disease onset, the authors suggest that they must be intrinsic to the disease process, and not secondary

changes. However, the RA disease process is likely to be initiated some time before symptomatic onset. A pivotal assumption of this paper is that CD45ROnull T cells reflect solely the naive population. Whilst this is broadly true, a more extensive phenotypic evaluation (eg using CD45RB, -RA, -RO and CD62L) would allow a more precise staging of T-cell differentiation. Future work should focus on the relationship between thymic activity and inflammation, and the thymic response to lymphodepletion. Additionally, thymus-stimulating cytokines could be studied as a means to rectify some of the observed abnormalities.

Methods

T-cell receptor excision circle (TREC) measurement, telomere terminal restriction fragment measurement

References

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