

University of Groningen

Dominant control region of the human β - like globin gene cluster

Blom van Assendelft, Margaretha van

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

1989

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Blom van Assendelft, M. V. (1989). *Dominant control region of the human β - like globin gene cluster*. s.n.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

SUMMARY

The structure and regulation of the human β -like globin gene cluster has been studied extensively. Genetic disorders connected with this gene cluster are responsible for human diseases associated with high levels of morbidity and mortality, such as β -thalassaemia and sickle cell anaemia. The work described in this thesis is concerned with a novel tissue-specific regulatory element. The human β -globin Dominant Control Region (DCR) confers integration-site independent, copy-number related, high-level expression to a linked β -globin gene in a tissue-specific manner in transgenic mice (see Chapter 2) and mouse erythroleukemia (MEL) cells (Chapter 3). The discovery of the human β -globin DCR sequences is an important step towards somatic gene therapy for thalassaemia and sickle-cell patients (Chapter 5).

The globin DCR as originally cloned in the "mini-locus" cosmid construct spans 33kb of DNA sequences. Deletion constructs were made to determine different functional areas within the DCR sequences (Chapter 3 and 4). It is now thought that the DCR functional elements are located within defined regions (as discussed in Chapter 5) characterized by the presence of strong DNase I hypersensitive sites (Chapters 2 and 3).

The human β -globin DCR can confer high level expression to other erythroid genes, namely the human α - and γ -globin genes (Chapter 5), and non-erythroid genes such as Thy-1 and tk-neo (Chapter 3).

The recent discovery of a region 3' flanking to the human T-cell specific CD2 gene with functional properties similar to those of the human β -globin DCR (discussed in Chapter 5) suggests that expression of other tissue-specific genes might also be regulated by DCR-like elements.