Blood Cells, Molecules and Diseases 70 (2018) 1

Contents lists available at ScienceDirect

Blood Cells, Molecules and Diseases

journal homepage: www.elsevier.com/locate/bcmd

Globins, from Genes to Physiology and Diseases

Douglas Vernimmen

The Roslin Institute, Developmental Biology Division, University of Edinburgh, Easter Bush, Midlothian EH25 9RG, UK

Oxygen capture (in unicellular) and delivery in (multicellular) organisms are vital for cellular function. Hence, it is no big surprise that many scientists have been interested in oxygen-binding proteins. A few years after the First World War, Alfred Mirsky (1900–1974) published eight papers on haemoglobin with Mortimer Louis Anson, while working in the laboratories of Joseph Barcroft and Lawrence Henderson at Harvard University (1924–1925). Mirsky's PhD thesis (1926) entitled "*The Haemoglobin Molecule*" showed that haemoglobin denaturation was a reversible process and the molecular structure was determined by Max Perutz in 1959. This basic biochemistry research was ground breaking, as it became very important a few decades later to understand the nature of some anaemia.

Although another scientist from the same generation, Conrad Hal Waddington (1905–1975), coined the term 'epigenetics' to describe heritable changes in gene expression that are not caused by changes in the DNA sequence (epigenetic landscape in "*The Strategy of the Genes*", 1940), Mirsky (again) was also the first pioneer in the field of molecular epigenetics as he showed that histone modifications have important roles in the regulation of transcription of chromatinised genomes (1964).

At the same time (1965), David Weatherall characterized the molecular basis of some forms of inherited anaemia (thalassaemia) and showed that these were due to the deletion of globin genes. Structural abnormalities of haemoglobin (sickle cell anaemia) had been described earlier, in 1949 by Linus Pauling (1901–1994), as well as the association with malaria resistance in 1954, by Anthony Allison (1925–2014).

Further characterization of the molecular basis of thalassaemias in patients, led to the identification of regulatory elements controlling the β- and α-globin loci by the groups of Frank Grosveld (1948-) and Doug Higgs (1951-) in 1983 and 1990 respectively. Since these original observations, remote regulatory elements have been identified for most genes. This has been a very active area of research after the sequencing of the human genome (2003) and more recently annotation of the regulatory elements by ENCODE and other consortia in 2012.

As we celebrate about 100 years of haemoglobin research, this Special Issue in *Blood Cells, Molecules and Diseases* aims to cover all aspects of globins, from the origin of the genes, their evolution, the variety of proteins they produce and the haemoglobinopathies due to qualitative (sickle cell anaemia) and quantitative (α- and β-thalassaemia) changes in globin expression. The classic and latest treatments, including epigenetic therapy (epi-drugs), which modulates the transcriptional activity of globin genes through DNA methylation and histone modifications will be described, as well as the most recent advances in gene replacement and gene editing. The last article of this Special Issue will examine how haemoglobin can be replaced by artificial molecules (synthetic blood), revolutionising the treatment of anaemia or of any patient in need of transfusion.

Retrospectively, this is a unique historical example of a fascinating research interest that has, over a century, revealed so many molecular bases of biology and human disease.

http://dx.doi.org/10.1016/j.bcmd.2017.02.002