



The Insulin peptide family

Author: Pierre De Meyts

Author title: MD, PHD, F.A.C.E.



Novo Nordisk
Pharmatech A/S



Insulin is only one member of a family of peptide hormones and growth factors that comprises 10 members in humans: insulin, insulin-like growth factors I and II (IGF-I and II) and seven peptides related to relaxin (Fig. 1).

They result from successive duplications of an ancestral gene that appeared early in animal evolution. Invertebrates also have many insulin-like peptides, e.g. 37 in the worm *C. elegans* and seven in the fruit fly *Drosophila Melanogaster* (1).

They play an important role in metabolism, growth, reproduction and longevity.

Figure 1: Canonical structure of members of the insulin peptide family. A. Insulin in the T conformation (PDB file 9INS). B. Insulin in the R conformation (PDB file 1ZNJ). C. IGF-I (PDB file 1GZR). D. IGF-II (PDB file 1ZNJ). E. Relaxin (PDB file 6RLX). The A-chains or A-domain are shown in blue, the B-chain or B-domain are shown in light green, the C-domain is shown in dark blue, and the E-domain is shown in light blue. The disulphide bridges are shown in yellow.

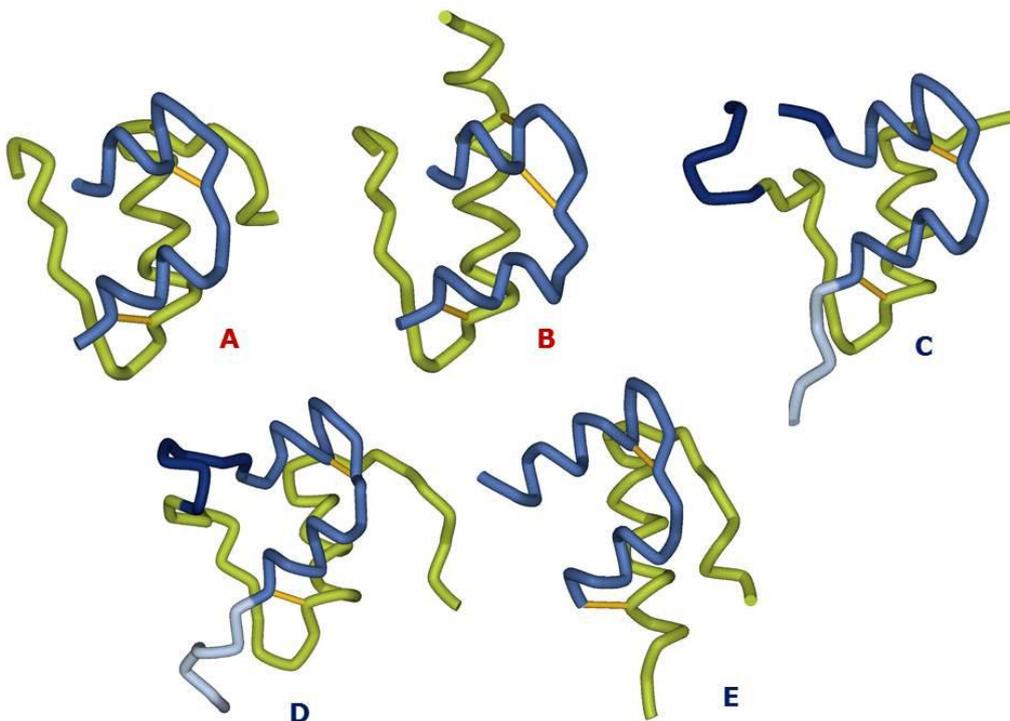


Figure 1

A bit of history

Insulin was isolated and purified for the first time to a grade suitable for treating diabetic patients at the University of Toronto in 1921 (2, see ref. 3 for a detailed history), winning the Nobel Prize in 1923 to Frederick G. Banting (1891-1941) and John J.R. McLeod (1876-1935). Besides being a life-saving therapy for diabetic patients, insulin turned out to be a bonanza for scientists interested in the structure and chemistry of proteins and provided many technological milestones. Insulin was the first protein to be sequenced by Frederick Sanger (born 1918) in Cambridge (4), winning him his first Nobel Prize in Chemistry in 1958. It was the first protein to be made by total synthesis in the early 60's independently by three groups: Panayotis Katsoyannis in New York (5), Helmut Zahn (1916-2004) in Aachen, Germany (6) and Yu Can Du and colleagues in Shanghai and Beijing (7). It was the first protein to be assayed by radioimmunoassay, developed by Rosalyn S. Yalow (1921-2011) and Solomon A. Berson (1918-1972) in New York. This achievement won the Nobel Prize in Physiology and Medicine to Yalow in 1977. Human insulin became the first protein made by recombinant DNA technology (see section on insulin bioengineering) to be produced commercially in 1982 (8).