INTRODUCTION

Somatomedin is a general term which refers to plasma factors that have both growth-promoting (stimulate sulfate incorporation into chondroitin sulfate of cartilage and increase thymidine incorporation into DNA in various tissues) and insulin-like effects (in adipose tissue and diaphragm, not neutralized by anti-insulin serum)\(^1,2\). "Somato" relates to somatotropin (growth hormone, GH) and also to the soma which is the target and "medin" to indicate it mediates the action of GH.

MOLECULAR FORMS OF SOMATOMEDINS

Many preparations have been designated as somatomedins. Somatomedin-A stimulated sulfate incorporation into glucosaminoglycans (sulfation factor activity) in chick cartilage\(^3-5\). Somatomedin-B stimulated DNA synthesis in glial cells\(^6\). Somatomedin-C had sulfation factor activity in rat cartilage\(^7\). Multiplication-stimulating activity had mitogenic activity in several cell types\(^8\). As radioimmunoassay for insulin was developed, it became apparent that human serum contained more insulin-like activity (ILA) than could be attributed to its content of immunoreactive insulin. The portion of ILA that was not inhibited by insulin antibodies was designated "atypical insulin", and "nonsuppressible insulin-like activity" (NSILA)\(^9,10\), which yielded two active peptides, NSILA I and II\(^11,12\). One portion of
NSILA was later shown to consist of insulin-like growth factors I and II (IGF-I and -II)\textsuperscript{11,12}. Another ILA was found to be similar to IGF-II\textsuperscript{13}. All of these substances were isolated from human plasma except for multiplication-stimulating activity, which was derived from the rat liver cell line, BRL 3A. Somatomedin-A appears to be identical to IGF-I, with the possible exception of a glutamine deamidation at position 40\textsuperscript{14}. Sequence analysis of somatomedin-C indicates that it is identical to IGF-I\textsuperscript{15}, and the term somatomedin-C/IGF-I (Sm-C/IGF-I) is now used to designate this peptide. Purification and analysis of one of the multiplication-stimulating activity fractions has revealed 93% homology with human IGF-II\textsuperscript{16}, so this peptide is now considered to be rat IGF-II\textsuperscript{17}. Somatomedin-B is not included among the somatomedins, since its mitogenic activity is due to contamination by epidermal growth factor\textsuperscript{18}.

Thus, the substances now considered to be members of the somatomedin group as determined by purification, sequencing and immunological characterization and receptor reactivity are limited to Sm-C/IGF-I or IGF-I and IGF-II. However, there may be other peptides which have not yet been characterized. For example, a "big IGF-II" has been reported in human spinal fluid and serum\textsuperscript{19}. This, and isolation of the somatomedins from plasma, and the study of cDNAs\textsuperscript{20,21} make it evident that there are more somatomedins that need further study.

IGF-I is a basic peptide with a MW of 7649; it contains 70 amino acids in a single chain with three disulphide bridges, is highly growth hormone dependent and has potent growth-promoting activity\textsuperscript{22-24}. IGF-II is a slightly acidic, single chain peptide with a MW of 7471; it contains 67 amino acids, appears to be less growth hormone dependent, and has less growth-promoting activity than IGF-I\textsuperscript{25,26}. Both IGF-I and -II have high structural homology with human proinsulin; they consist of A, B, C and D domains. Parts of the sequences within the A and B domains are homologous to the A and B chains of insulin, with their interchain disulfide bridges. This sequence homology is 43% for IGF-I and 41% for IGF-II. No sequence homology exists between the C domains of IGF-I and -II (12 and 8 amino acids, respectively) and the C peptide region (35 amino acids) of human proinsulin\textsuperscript{27-30}. In addition, the carboxyl-terminal extensions (D domains) of 8 and 6 amino acid residues are, respectively, typical structural features of IGF-I and -II which are not shared with proinsulin\textsuperscript{27-29}. IGF-I has a 130-residue precursor, whereas the IGF-II has a 180-residue precursor\textsuperscript{30a}. The sequence homology between IGF-I and -II is 62%. Three-dimensional models for IGF-I and -II indicate identical three