The relationship between the L1 and L2 domains of the insulin and epidermal growth factor receptors and leucine-rich repeat modules

ABSTRACT

The leucine-rich repeat superfamily comprises right-handed beta helix proteins like pectate lyase and the L domains of members of the insulin receptor and epidermal growth factor receptor families, as indicated by multiple sequence alignments and comparisons between different 3D structures.

INTRODUCTION

Insulin is a hormone secreted from the pancreas to stimulate the production of glucose in the blood. The insulin is released from the pancreas into the bloodstream, where it is divided into two parts – insulin-like growth factor (IGF)-I (IGF-I is the hormone secreted by the pancreas to stimulate the growth of muscle, and IGF-I is the growth factor involved in the muscle growth process) and IGF-II (IGF-II, the growth factor involved in the muscle growth process) – which then enter the blood stream and are synthesized into IGF-I and IGF-II. Both IGF-I and IGF-II are produced in the liver as a result of glucose utilization. However, Many proteins exhibit a modular structure and are composed of various structural elements, including immunoglobulin domains, EGF-like repeats (like epidermal growth factors), fibronectin type 3, and leucine-rich repeat structures. Some evidence indicates that the L domains in the IR and EGFR families are highly leucine-rich repeats, with legucine being the most common residue at 10-16%. The 3D structure of the IGF-1R's L1/cys-rhod2 fragment shows that these Ldomains are single-stranded right-handed (although they have some structural similarities to pectate lyase and right–handed) beta-alpha superhelix proteins. Among the six subfamilies of leucine-rich repeat proteins, typical, RI-like, conspecific, phytosanitary, SD22 and bacterial have their own unique lengths and consensus sequences. The diversity in sequence motifs among LRR proteins led to re-examining the sequences of the L1 and L2 domains belonging to the IR and EGFR families. While the single LOR motif is challenging to identify, it becomes more easily recognizable when analyzing multiple sequence alignments. The identification of conserved sequence patterns was significantly aided by the availability of IGF-1R L1, L2, and pectate lyase, as well as the known LSR proteins RI and internalin 1B.

CONCLUSION

Using a combination of sequence analyses and 3D structure comparisons, we have demonstrated that the L domains of members of the IR and EGFR subfamilies, as well as those of other LRRs such as porcine ribonucleases, exhibit variations of this typical repeating motif.