

The LRR and TM Containing Multi-Domain Proteins in Arabidopsis

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1. Introduction

Thousands of different multi-domain proteins, each the product of one separate specific gene, which exhibit one or multiple transmembrane (TM) domains, are expressed in Arabidopsis as well as in Homo sapiens (Sallman-Almen et al.,2009). These molecules may carry one or multiple TM domains very close to the amino or carboxyl terminus or even dispersed throughout the molecule Thus one may conclude that the TM domain existed prior to the branching of plants and metazoa. In both organisms, a very small percent of the TM domain containing proteins additionally possess multiple leucine rich repeats (LRR) domains. These domains seem to transmit ligand perception. So one should presume that such domains also existed prior to the branching of these two forms of life. (A caveat, however, is in order: Many of the combinations of the various domains which one finds in plants are not present in the same combination in animals and vice versa.). As demonstrated in this paper, subsequently, during evolution, on several occasions, the genes for these multi-domain proteins duplicated and during this process they were often altered slightly to allow generation of proteins that could provide new specific functioning (i.e.they underwent neofunctionalization).

Unlike the “adaptive immune” system which exists in animals but not in plants, an “innate immune” system is present in all multicellular organisms (animals and plants). This latter system operates by way of receptors: the Toll-like receptors (TLRs) (first identified in Drosophila) which bind lipopolysaccharides (endotoxins). In Drosophila, these receptors not only activate innate immunity; they also act in dorsal-ventral specifications. When one compares these molecules as they are encoded e.g. in Arabidopsis (Dangl & Jones, 2001) with those present in Homo Sapiens, one finds that in animals – but not in plants – these receptor proteins possess a cysteine rich domain just prior to entering the membrane and also a signaling domain (which is not a protein kinase but which acts as a docking site) on the backside of the TM domain. TLRs target “pathogen associated molecular patterns” (PAMPs) by way of the LRRs domains.

There are, however, besides of TLRs, many other multi-domain proteins that contain both TM and LRR domains, encoded in Arabidopsis and also in Homo sapiens. Many exist in both of these two species but some of them are present only in one or in the other. Below we list more than a hundred of these various proteins (each expressed from an individual gene) present in Arabidopsis. The TM domain is an about 22 AA residue domain and the LRR is an about 20-29 residue domain (which contains about 6 Leu). Both domains are present in proteins that

participate in protein-protein interactions but which have different functions and cellular locations. In each case, the protein is presented below, in an order guided by a Clustal X arrangement (<http://www.clustal.org/>) and is labeled by its NCBI (<http://www.ncbi.nlm.nih.gov/protein>) protein identification number, followed by its chromosomal locus tag, in diagram form as given by SMART (<http://smart.embl-heidelberg.de>).

1.1 Proteins with extracellular multiple LRR domains, a single TM domain (blue rectangle) positioned close to the carboxyl terminus and a short cytoplasmic tail



NP_199740;AT5G49290; Protein Binding



NP_177558;AT1G74180; Receptor Like Protein 14; Protein Binding



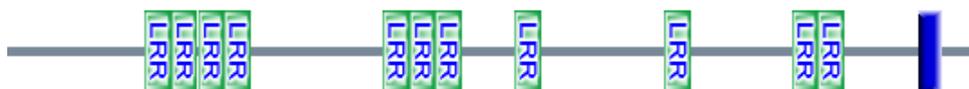
NP_180117;AT2G25470; Receptor Like Protein 21; Protein Binding
(NP_199740, NP_177558 and NP_180117 display 60% AA identity.)



NP_177559;AT1G74190; Receptor Like Protein 15; Protein Binding



NP_177557;AT1G74170; Receptor Like Protein 13; Protein Binding



NP_190892;AT3G53240; Receptor Like Protein 45; Protein Binding



NP_176115;AT1G58190; Receptor Like Protein 9, Protein Binding



NP_178125;AT1G80080; TMM (Too Many Mouths); Protein Binding/Receptor. (Note: This protein promotes cell fate progression in stomatal development of stems (Bhave et al.,2009)).



P_176717;AT1G65380; Clavata 2; Protein Binding /Receptor Signaling Protein. (This protein forms a distinct CLE binding receptor complex regulating stem cell specification (Guo et al.,2010)).



NP_188941; AT3G23010; Receptor Like Protein 36 (Disease Resistance Protein)



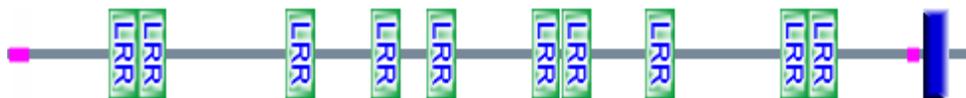
NP_187188; AT3G05370; Receptor Like protein 31; Protein Binding



NP_177296; AT1G71400; Receptor Like Protein 12; Protein Binding



NP_567412;AT4G13920; Receptor Like Protein 50; Protein Binding



NP_197963; AT5G25910; Receptor Like Protein 52; Protein Binding (Note: It is a putative disease resistance protein induced e.g. by chitin oligomers (Ramonell et al., 2005)).



NP_187719; AT3G11080; Receptor Like Protein 35; Protein Binding



NP_187712; AT3G11010; Receptor Like Protein 34; Protein Binding



NP_189531; AT3G28890; Receptor Like Protein 43; Protein Binding



NP_187217; AT3G05660; Receptor Like Protein 33; Protein Binding



NP_179112; AT2G15080; Receptor Like Protein 19; Protein Binding

Note: It is possible that the primary function of most – if not of all – of the proteins listed above is to provide disease resistance.

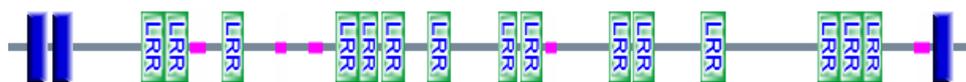
1.2 Proteins with one single TM domain positioned at the amino terminus and another one close to the carboxyl terminus



NP_198058:AT5G27060; Receptor Like Protein 53; protein binding



NP_187216:AT3G05650; Receptor Like Protein 32; protein binding



NP_175225:AT1G47890; Receptor Like Protein 7; protein binding. Note: NP_175225 possesses two TM domains at the AA terminus. (NP_198058, NP_187216 and NP_175225 exhibit 44 % AA identity.)



NP_188953:AT3G23120; Receptor Like Protein 38; protein binding:



NP_188952:AT3G23110; Receptor Like Protein 37; protein binding



NP_187187:AT3G05360; Receptor Like Protein 30; protein binding



NP_177295:AT1G71390; Receptor Like Protein 11; protein binding



NP_180864;AT2G33050; Receptor Like Protein 26; protein binding . Notice loss of carboxyl terminal TM.



NP_173167;AT1G17240; Receptor Like Protein 2; protein binding

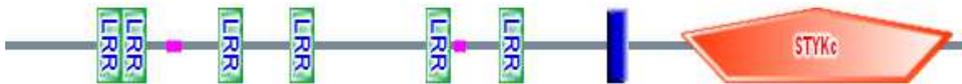


NP_173168;AT1G17250; Receptor Like Protein 3; protein binding

2. Receptor Like Kinases (RLKs)

2.1 Proteins with extracellular N-terminal LRR domains, a TM domain and an intracellular STYKc (tyrosine kinase catalytic) domain which is close to the C-terminus

These proteins are expected to play roles in intercellular communication during tissue identity maintenance and regulation of development. Still some of them have been shown to play a role in innate immunity. Interaction with the extracellular LRR domains results in activation of the intracellular STYK catalytic domain. Then, the activated receptor, in response, catalyses the phosphorylation of tyrosine residues in intracellular proteins.



NP_191196;AT3G56370; Leucine rich repeat transmembrane protein kinase. (Inflorescence and root apices receptor-like kinase (IRK). (Hattan et al., 2004)



NP_195809;AT5G01890; Leucine rich repeat transmembrane protein kinase



NP_189443;AT3G28040; Leucine rich repeat transmembrane protein kinase



NP_172708;AT1G12460; Leucine rich repeat transmembrane protein kinase



NP_193747;AT4G20140; Leucine rich repeat transmembrane protein kinase.

(GASSHO 1).



NP_199283;AT5G44700; Leucine rich repeat transmembrane protein kinase.

(GASSHO 2). (GASSHO 1 and 2 show 76% AA homology. They are required for the formation of normal epidermal surface during embryogenesis (Tsuwamoto et al., 2008).



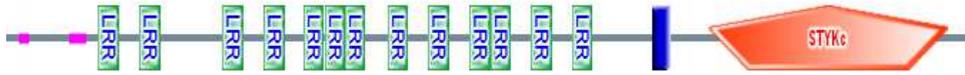
NP_201371;AT5G65700; Leucine rich repeat transmembrane protein kinase. (BAM1/ Barely any meristem 1). Bam receptors regulate stem cell specification and organ development through interactions with Clavata signaling (DeYoung & Clark,2008).



NP_190536;AT3G49670; Leucine rich repeat transmembrane protein kinase. (Bam2)



NP_193760;AT4G20270; Leucine rich repeat transmembrane protein kinase (Bam3). BAM 1,2 and 3 exhibit 49% AA identity). Notice the presence of a second TM at the amino terminus of Bam 3 which evolution diluted for Bam 1 and 2.



NP_180875;AT2G33170; Leucine rich repeat transmembrane protein kinase



NP_174166;AT1G28440; ATP binding/protein serine/threonine kinase (HAESA-Like1)



NP_194578;AT4G28490; ATP binding/protein serine/threonine kinase (HAESA)



NP_201372;AT5G65710; ATP binding / protein serine/threonine kinase (HAESA-Like2) The three HAESA proteins function in developmentally regulated floral organ abscission (Jinn et al., 2000). (NP_174166, NP_194578 and NP_201372 exhibit 37% AA identity.)



NP_197965;AT5G25930; Leucine rich repeat family protein kinase



NP-199777;AT5G49660; Leucine rich repeat transmembrane protein kinase



NP_188604;AT3G19700; ATP binding / protein kinase (Haiku 2) Haiku 2 may play a role in the determination of seed size by endosperm (Garcia et al.,2003).



NP_178330;AT2G02220; ATP binding / protein kinase (Phytosulfokine (PSK) Receptor 1).PSK may play a role in pathogen or herbivore interactions (Loivamaki et al.,(2010) (NP_188604 and NP_178330 exhibit 29.3% AA identity.)



NP_196311;AT5G06940; Leucine rich repeat family protein



NP_190342; AT3G47580; Leucine rich repeat transmembrane protein kinase



NP_190293; AT3G47090; Leucine rich repeat transmembrane protein kinase



NP_566892; AT3G47570; Leucine rich repeat transmembrane protein kinase



NP_190295; AT3G47110; Leucine rich repeat transmembrane protein kinase



NP_197548; AT5G20480; ATP binding / protein kinase (EF-TU receptor) It recognizes bacterial PAMP EF - Tu. (Zipfel, et al., 2006).



NP_199445;AT5G46330; ATP binding / protein kinase (Flagellin sensitive 2 (FLS)).It recognizes bacterial flagellin and evokes plant innate immunity (Lu, et al., 2010)



NP_180150;AT2G25790: Leucine rich repeat / transmembrane protein kinase



NP_178304;AT2G01950; BRI1-like2 ATP binding / protein serine-threonine kinase. This kinase interacts with vascular-specific adaptor proteins to influence leaf venation. (Ceserani et al.,2009.) Note absence of amino terminal TM.



NP_187946;AT3G13380; BRI1-like3 ATP binding / protein serine-threonine kinase. Note absence of amino terminal TM.



NP_195650;AT4G39400; Brassinosteroid insensitive 1 (BRI1) ATP binding / protein serine-threonine kinase. (Brassinosteroids regulate plant development by way of a signal transduction pathway involving BRI1 and BAK1 transmembrane receptor kinases (Wang et al., 2008).



NP_175957;AT1G55610; BRI1-like1 ATP binding / protein serine threonine kinase.



NP_196345;AT5G07280; EMS1 (Excess Microsporocytes 1) Transmembrane receptor protein kinase. (This protein controls somatic and reproductive cell fates in the anther of Arabidopsis.) (Zhao et al., 2002) Note absence of the amino terminal TM.



NP_178330;AT2G02220; Phytosulfokine receptor (PSK R1) ATP binding / protein serine-threonine kinase. (PSK represents a class of hormones that affects cellular longevity and growth (Matsubayashi et al., 2006).



NP_200200;AT5G53890; Leucine-rich repeat transmembrane protein kinase



NP_181713;AT2G41820; Leucine-rich repeat transmembrane protein kinase



NP_174702;AT1G34420; Leucine rich repeat transmembrane protein kinase



NP_177694;AT1G75640; Leucine rich repeat transmembrane protein kinase



NP_193826;AT4G20940, Leucine rich repeat transmembrane protein kinase

Note: For molecules such as NP_172468 SMART does not recognize any LRR regions. Hence, these molecules are not listed here.

2.2 The members below possess a TM domain at the amino terminus and a second one in front of the STYKc domain:



NP_201029;AT5G62230; Erecta - like 1 (ERL1); kinase. Mediates morphological alterations. (Uchida et al.,2011).



NP_196335;AT5G07180; Erecta - like 2 (ERL 2); kinase



NP_173217;AT1G17750;Leucine rich repeat / transmembrane protein kinase. PEP receptor 2 (PEPR2). The amino terminal TM is lost (overly mutated).



NP_177451; AT1G73080; ATP binding / protein serine/ threonine kinase, PEP1 receptor (PEPR1). (PEP1 and 2 are implicated in Arabidopsis development and immunity) (Postel, et al.,2010). (PEPR1 and PEPR2, both perceive the existence of an endogenous danger signal Peptide 1 when such a peptide is present.) (Krol et al.,2010). (NP_173217 and NP_177451 exhibit 70% AA identity.)



NP_199705;AT5G48940 Leucine rich repeat transmembrane protein kinase



NP_189066;AT3G24240; Leucine rich repeat transmembrane protein kinase



NP_200415;AT5G56040; Leucine rich repeat transmembrane protein kinase



NP_201198; AT5G63930; Leucine rich repeat transmembrane protein kinase



NP_174809; AT1G35710; Leucine rich repeat transmembrane protein kinase



NP_192625, AT4G08850; Leucine rich repeat transmembrane protein kinase

NP_200956; AT5G61480; Leucine rich repeat transmembrane protein kinase..PXY receptor.
(This receptor like-kinase is essential for polarity during plant vascular tissue development.
(Fisher & Turner, 2007))

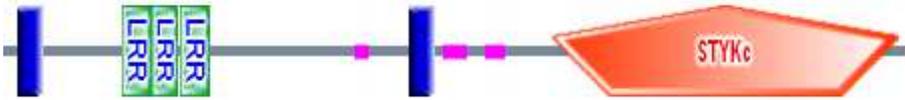
NP_176483; AT1G62950; Leucine rich repeat transmembrane protein kinase



NP_565084; AT1G74360; Leucine rich repeat transmembrane protein kinase

NP_177374; AT1G72300; Leucine rich repeat transmembrane protein kinase, (This protein
"perceives" phytosulfokines (Amano et al., 2007)).

NP_190742; AT3G51740; Inflorescence Meristem Receptor-Like Kinase (IMK2)



NP_201529;AT5G67280; Receptor-Like Kinase (RLK)

The Strubbelig Receptor Family Kinases:



NP_196300;AT5G06820; (SRF2) Strubbelig receptor family 2; kinase. An amino terminal TM is lost. SRFs affect the formation and shape of several organs by influencing cell morphogenesis, the orientation of the division plane and cell proliferation. (Chevalier et al., 2005).



NP_566444;AT3G13065; (SRF4) Strubbelig receptor family 4; kinase



NP_178019;AT1G78980; (SRF5) Strubbelig receptor family 5, kinase . The amino terminal TM is lost.



NP_175777;AT1G53730; (SRF6) Strubbelig receptor family 6; kinase



NP_188052;AT3G14350; (SRF7) Strubbelig receptor family 7; kinase.. The amino terminal TM is lost.

Not shown:

NP_565489;AT2G20850; (SRF1) Strubbelig receptor family 1; kinase. All LRR domains are lost. (SMART).

NP_192248;AT4G03390; (SRF3) Strubbelig receptor family 3; kinase. The amino terminal TM is duplicated. All LRR domains are lost. (SMART).

NP_193944;AT4G22130; (SRF8) Strubbelig receptor family 8, kinase. All LRR domains are lost.(SMART).

Note: For molecules such as NP_177363 SMART does not recognize any LRR regions. Hence, these molecules are not listed here.

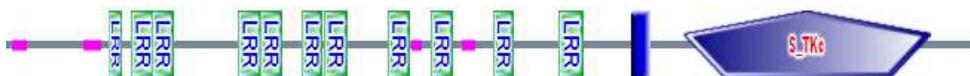
3. Proteins that contain an S_TKc domain: (AA homology is 44% for S_TKc vs. STYKc.)



NP_173166;AT1G17230; Leucine rich repeat / transmembrane protein kinase



NP_174673;AT1G34110; Leucine rich repeat / transmembrane protein kinase



NP_567748;AT4G26540; Leucine rich repeat / transmembrane protein kinase



NP_195341;AT4G36180; Leucine rich repeat / transmembrane protein kinase

4. Conclusion

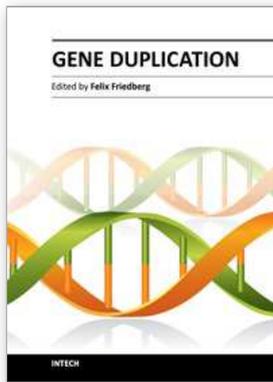
Gene duplication is rampant. It should be noted that the products depicted above show considerable variation both in number of, and distances between, the LRR domains. Where, when and how do the genes listed here function? For most of them there is no evidence that they deliver innate immunity in the plant. Of course, some of them do! For many the function is not known. Gene duplications, carrying amino acid changes resulting from mutations, often end in neofunctionalization even though duplicate genes may also merely provide tissue specific expression for the original ancestral gene. Subsequent alternate splicing of genes, in turn, might also give new roles to the genes. But if domains are the units that built proteins, then domain shuffling provides a more efficient source for expressed gene versatility: (Thereby, nature promotes evolution of disparate proteins for novel functions.) Most of the genes listed in this chapter certainly exist because of duplication. These genes could be grouped further, however, because another domain had first been added for the projected protein molecules, long before the gene duplications occurred. Possibly, domains represent the evolutionary building blocks for all proteins. At present we can only speculate as to the mechanism of such random multi-domain protein formation. Were transposons involved? (Retroproession, the process that is responsible for pseudogene formation, possibly could have also facilitated the creation of new disparate proteins!). Specific domain combinations might have been built randomly - maybe sometimes just once during the evolution of an organism - and then sometimes only to be rearranged during duplication or even to loose domains by mutating them away thereafter. (.See e.g..the Strubbelig family members 1-8.)

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The book Gene Duplication consists of 21 chapters divided in 3 parts: General Aspects, A Look at Some Gene Families and Examining Bundles of Genes. The importance of the study of Gene Duplication stems from the realization that the dynamic process of duplication is the "sine qua non" underlying the evolution of all living matter. Genes may be altered before or after the duplication process thereby undergoing neofunctionalization, thus creating in time new organisms which populate the Earth.

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