ISSN (Print 0974-2115) (Online 2349-8552)
www.jchps.com Journal of Chemical and Pharmaceutical Sciences

A Brief Overview on Early Events of Xa21 Mediated Pattern Triggered Immunity

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ABSTRACT

In plant associated pattern-triggered immunity (PTI), pattern-recognition receptors (PRRs) play crucial role in the mechanism of first line of defense against pathogenic invasion. Throughout the event, PRR binds with microorganism's pathogen-associated molecular pattern (PAMP) and recruit co-receptor protein to initiate the primary defense signal. Although several plant PRRs have been identified, very few of them have been fully characterized and studied so far. PRR Xa21 perceives PAMP RaxX21 and activates pattern triggered immunity in *Oryzae* spp (rice). The early events regulated by Xa21 is mainly binding of it with PAMP RaxX21 as well as recruit a co-receptor protein OsSerk2. This review article elucidates the steps of activating first line of defense mechanism of rice plant arbitrated by PRR Xa21.

KEY WORDS: PRR, PAMP, PTI, Xa21, Defense

1. INTRODUCTION

The first layer of defense mechanism in plant is referred as pattern triggered immunity (PTI) (Jones, 2006; Ronald, 2010; Tsuda, 2009). Plant has many immune receptors which are localized at cell surface. These receptors play a vital role in PTI. These receptors perceive pathogen associated molecular pattern (PAMPs) or microbial associated molecular pattern (MAMPs) secreted by microorganisms like bacteria, fungi etc. These PRRs are mainly two types. One is receptor like kinase (RLK) which has kinase domain at the end and another one is receptor like protein (RLP) which does not have any kinase domain (Zipfel, 2014). Receptor like kinase has four main region which are leucine rich repeat (LRR), a single pass transmembrane domain (TM), one juxtamembrane domain (JM) and an intracellular kinase domain (Song, 1995). The LRR binds with PAMPs/MAMPs and through the TM and JM the signal is transferred to the inner side of the cell by kinase domain and PTI is activated. During this event a co-receptor protein is recruited which is required for the fill activation of PTI (Chen, 2014).

Successful pathogens can avoid the pattern triggered immunity and secrets effectors by its type 3 secretion system (Thomma, 2011). Plant can also avoid harmful activities caused by effectors by its resistant proteins R. Most of these proteins are intracellular receptor proteins of the nucleotide binding leucine rich repeat (NB-LRR). Effector triggered immunity occur more rapidly than pattern triggered immunity (Tao, 2003; Tsuda, 2010). These effectors previously known as avirulence factors (Chisholm, 2006; Bent, 2007). This ETI is also known as gene-for-gene hypothesis where both gene product from plant and pathogen interacts with each other in a receptor-ligand manner (Schurch, 2004).

Rice Xa21 is a of PRR-RK falls under the XII sub-family (LRR-RK XII) with the other two best characterized PRR-RKs *Arabidopsis* FLS2 and EFR (Holton, 2015). Sub-family XII is one of the most expanded subfamily of LRR-RK in rice which encodes mostly for PRRs or PRR-associated RKs due to presence of non-RD kinase domains (Dardick, 2006).

Due to the presence of Xa21, rice plant shows robust resistance to bacterial leaf blight (BLB) causing *Xanthomonas oryzae pv. Oryzae (Xoo)* (Wang, 1996; Ishiyama, 1922). BLB is regarded as one of the major diseases of rice (Swings, 1990), which can cause yield loss up to 70% (Mew, 2001). The best cost effective control of this disease is achieved by using of resistant cultivars (Nino-Liu, 2006; Pinta, 2013). This mini overview elucidates the initial steps of activating front line of defense mechanism arbitrated by PRR Xa21.

Brief overview of Pti Arbitrated by XA21:

Domains of Xa21: Xa21 has 23 leucine rich repeat (LRR) domains (Figure.1)**,** one transmembrane (TM) domain, one juxtamembrane domain (JM) and one kinase domain.

ISSN (Print 0974-2115) (Online 2349-8552)
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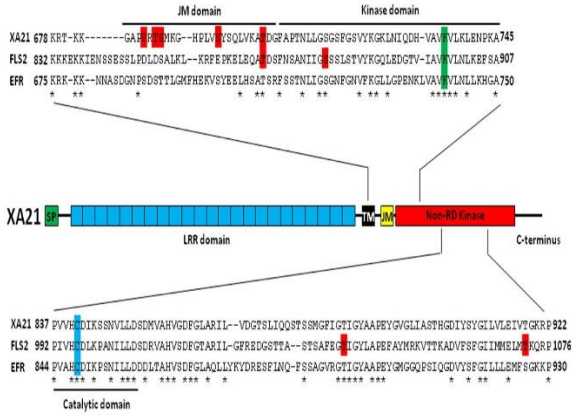

Figure.1. Detailed domain structures of Xa21 (Park, 2012)

LRR domain which is localized outside of the plant membrane, binds to bacterial peptide RaxX21 (Pruitt, 2015) where JM domain transfers the signal to kinase domain. This activates the PTI where co-receptor protein OsSerk2 associates with Xa21 helping to trigger the plant defense mechanism. Perhaps due to this, the in situ structural complexity of the whole protein, Xa21 structure is yet to be determined experimentally.

RaxX21-sY as activator of Xa21 mediated immunity: For the activation of Xa21 mediated immunity, six *Xoo* genes of two functional classes are required. RaxA, raxB and raxC which belongs to the first class, encode a membrane fusion protein (MFP), an adenosine triphosphate (ATP) binding cassette (ABC) transporter protein, and an outer membrane protein (OMP), respectively. These all together are predicted to comprise a type 1 secration system. *Xoo* Bacteria secrets RaxX21 through this type 1 secretion system (Figure.2) (Ronald, 2014). But before the secretion, this RaxX21 become sulphated with the help of another second class of rax genes raxP and raxQ (Shen, 2002). These encode an ATP sulfurylase and an adenosine 5'- phosphosulphate (APS) kinase and function in concert to produce 3'-phosphoadenosine 5'-phosphosulphate (PAPS), the universal sulfuryl group donor (Y shen 2002) (Figure.3).

This sulphation takes place at the 7th amino acid tyrosine of RaxX21. It is predicted that about 1% of all tyrosines are sulphated in eukaryotic cells where this sulphation plays a vital role as mediator in protein-protein interaction. The enzymes tyrosylprotein sulfotransferases or TPSTs catalyze the transfer of a sulfonate group from the donor compound 3'-phosphoadenosine 5'-phosphosulfate or PAPS to the hydroxyl group of a luminally oriented peptidyltyrosine residue to form a tyrosine O4-sulfate ester and 3',5'-ADP (Figure.3).

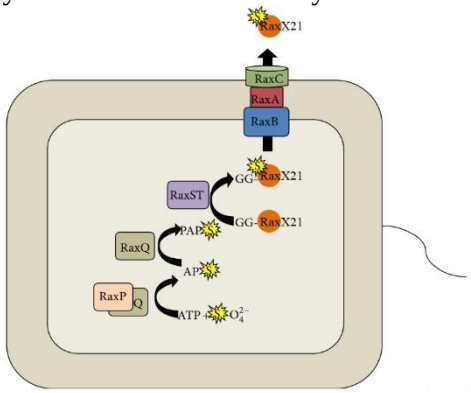

Figure.2. Synthesis and secretion of RaxX21 protein (Ronald, 2014)

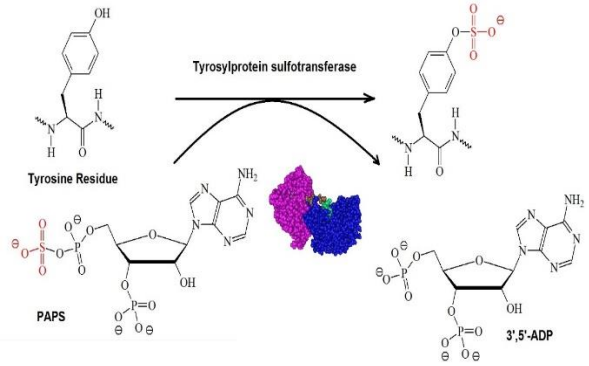

Figure.3. The tyrosylprotein sulfotransferase mechanism in RaxX21 7th AA (Biosynthesis, 2015)

Xa21 Leucine rich repeat domain recognize RaxX21-sY: Immediately after secretion of RaxX21-sY (sulphated RaxX21) by *Xoo* through type 1 secretion system, it is recognized by rice PRR Xa21 leucine rich repeat domain. Xa21, not having the transmembrane and kinase domains, shows partial resistance to bacterial blight. This proves that when RaxX21 binds with LRR of Xa21, in absence of transmembrane and kinase domain, an unidentified receptor kinase is activated which transduce the signal of defense mechanism which leads the plant to show partial resistance.

OsSerk2 Co-receptor regulates the Xa21 mediated immunity: In case of FLS2 and EFR mediated immunity BAK1 co-receptor protein positively regulates the innate immunity of the plant. When PAMP binds with FLS2 or EFR, it forms an instantaneous complex with BAK1. Like FLS2 and EFR, Xa21 and OsSerk2, a co-receptor protein (Figure.4) for Xa21 mediated immunity form a heterodimer complex upon recognition of RaxX21-sY.

Moreover, in case of FLS2 mediated immunity, the PAMP flg22 acts as a molecular glue by stabilizing the interaction between receptor FLS2 and co-receptor BAK1 (Sun, 2013). But in the case of Xa21 mediated immunity,

the strong association between Xa21 and co-receptor OsSerk2 without ligand treatment in mature rice plant proves that the association between Xa21 and OsSerk2 is PAMP independent.

Again, mutation in BAK1 Asp122 amino acid has altered interaction with the receptor FLS2 suggests that mutation in co-receptor protein OsSerk2 may have significant impact on its binding with Xa21. Later crystallographic structure of the OsSerk2 LRR domain and its mutant version (D128) proved that the mutation has significant impact on its intra-protein binding. In the wild type, the OsSerk2 Asp128 forms a salt bridge to Arg152 (McAndrew, 2014). But in mutant, Arg152 forms a salt bridge with the nearby residue Glu174 (Figure.5). This change in salt bridge formation may have significant impact on binding of the protein with its PRR Xa21 and thus may affect the resistance level of the plant.

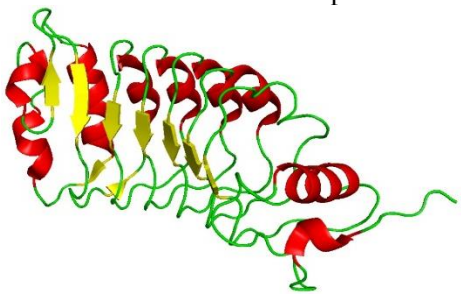

Figure.4. Cartoon representation of OsSerk2 structure (PDB ID: 4Q3G) (McAndrew, 2014)

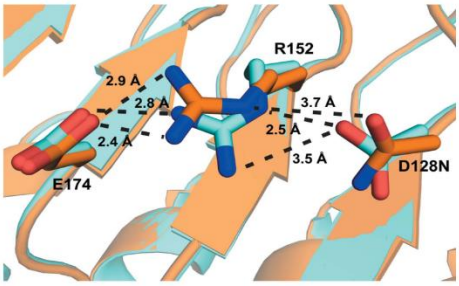

Figure.5. Salt bridge formation by OsSerk2 Arg152 with other residues (McAndrew, 2014)

JM domain and other proteins regulate Xa21 mediated immunity: JM domain of Xa21 protein plays vital role in regulation of Xa21 mediated immunity. Autophosphorylation of the residue Ser686, Thr688 and Ser689 has vital role in case of stabilizing the Xa21 protein. Mutation in any of this three amino acids show partial resistance to bacterial blight disease compared to wild type Xa21 (Xu, 2006). Also Thr705 in the JM region is required for binding of Xa21 protein with other regulatory protein XB3, XB10, XB15, XB24 (Chen, 2010).

Ring finger ubiquitin ligase XB3, which is trans phosphorylated by kinase domain of Xa21 is required for Xa21 mediated immunity (Wang, 2010). Moreover XB10, a WRKY transcriptional factor, can interact with kinase domain of Xa21 and can negatively regulate the Xa21 mediated immunity (Park, 2010).

Overexpression of XB10, a WRKY transcriptional factor suppress the expression of Xa21 mediated immunity and this negatively regulate the PTI mechanism in rice plant (Peng, 2008). Like XB10, another protein phosphatase XB15 negatively regulates the Xa21 mediated immunity (Park, 2008).

XB24 another ATPase interacts with Xa21 and regulates the immunity mediated by Xa21 (Chen, 2006). XB24 keeps Xa21 in dormant stage by promoting auto phosphorylation of certain Ser/Thr sites while physically associated with it. Upon recognition of RaxX21, XB24 dissociates from Xa21 and PTI mechanism is activated. Thus XB24 regulates the Xa21 before its interaction with RaxX21 while XB3, XB10 and XB15 controls the activity of Xa21 after recognition of RaxX21 by Xa21 (Figure.6).

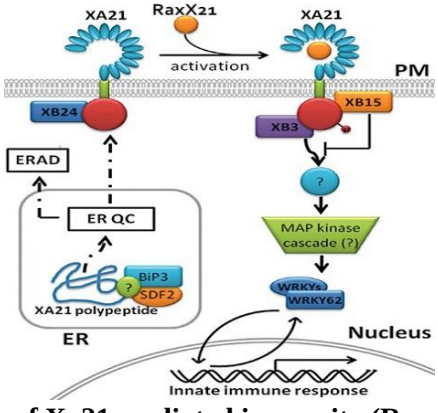

Figure.6. An overview of Xa21 mediated immunity (Ronald and Beutler, 2010)

2. CONCLUSION

Much of what has been experimented above describes an overview of PRR Xa21 along with its perception of bacterial PAMP RaxX21 and OsSerk2. Since, Xa21 has been shown to play a key role in pattern triggered immunity, clear understanding of its structural details is necessary before concluding its functional role in the disease defense mechanism. Future research can be carried out to retrieve the crystallographic structure of Xa21 and its interaction with RaxX21-sY as well as co-receptor OsSerk2 to deduce its functional detail on heterodimer PTI complex formation.

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