accelaration activity" or by binding protease factor I in "co-factor activity" to degrade C3b into inactive iC3b [7]. Non-protected labelled surface, on the other hand, trigger the terminal pathway of complement activation, which is started by cleavage of C5 (a homologue of C3) into C5b and association with MAC-protein C6 into C5b6. C5b6 in turn binds other MAC proteins C7, C8 [8] and multiple C9s causing MAC formation and cell lysis.

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Structural basis of disease resistance in flax against flax rust

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Plant diseases are a major issue for economical important crops worldwide. Plant immunity is triggered by the recognition of a pathogen effector protein by a plant resistance (R) protein, leading to the activation of plant defences, which often culminate in a localized cell death response.

The R proteins can be divided into a few conserved families, while the effectors are diverse in both sequence and structure, and have roles in virulence. Recognition of effectors by R proteins, and the subsequent activation and downstream signaling events, are poorly understood at the molecular and structural level. We have used the interaction between flax, and the fungal pathogen, flax rust, as a model system to characterize this process. The flax-R proteins consist of a central nucleotide-binding (NB) domain, a C-terminal leucine-rich-repeat (LRR) domain, and an N-terminal Toll-interleukin-receptor like (TIR) domain. The LRR domains of flax R proteins are involved in direct interaction with corresponding flax-rust effectors [1,3], while the NB and TIR domains have roles in activation and signalling, respectively.

Here, we report the first crystal structure of a TIR domain from a plant R protein (L6) at 2.3 Å resolution [4]. The structure reveals important differences from the structures of mammalian and bacterial TIR domains. Analysis of the structure combined with site-directed mutagenesis suggests that TIR domain self-association is a requirement for immune signaling, and reveals distinct surface regions involved in self-association, signaling, and autoregulation.

We have also determined crystal structures of two different variants of the flax rust-effector protein AvrM. One of these variants AvrM-A, is recognized by the M resistance protein in flax, which results in activation of a necrotic immune response. The second variant avrM, is not detected by M and promotes disease. Both structures have a novel L-shaped helical fold, with two chains forming a dimer with an unusual non-globular shape. Comparison of the two structures provides insight into the structural basis of effector recognition by R proteins.

Our results bring us a step closer to understanding the molecular basis for the disease resistance process in plants, which is a prerequisite for the future engineering of novel resistance specificities into commercially important crops.

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Structure of Complement C6 Suggests a Universal Model for Pore Formation by Cytolysins

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The Membrane Attack Complex (MAC) forms lytic pores in the outer membranes of Gram-negative bacteria. Pore formation begins with conversion of C5 to C5b, which promotes assembly of an initiation complex on the membrane surface comprising 4 structural elements: C6, C7, C8 α and C8 β, each of which contains a "MACPF" domain, a building block of the circular pore. This complex then recruits ~10 copies of a 5th MACPF domain protein, C9 forming membrane-spanning β-barrel. The transformation of MACPF domain from a pre-pore to a pore conformation leads to unwinding of two helical subdomains, CH1 (TMH1) and CH2 (TMH2), to form transmembrane β-hairpins. The structural and regulatory principals of initiation and propagation of assembly and membrane insertion are poorly understood. Each structural protein has "auxiliary" domains N- and C-terminal to the MACPF domain whose role has thus far been unclear. Here we describe the atomic resolution structure of full-length C6, the longest of the structural proteins, which shows how N- and C-terminal auxiliary domains cooperate to stabilize a "closed" conformation of the central β-sheet of the MACPF domain, while locking the membrane-inserting elements into their "pre-pore" state. On the basis of structural comparisons with C8 and perforin, we propose a model in which the "opening" of the β-sheet is key to initiating and propagating assembly. We show that only open conformations of the β-sheets are capable of forming a circular concatamer in which the edges of each β-sheet are shared with its neighbors, forming a single contiguous barrel. As the pore is constructed, the exposed edge of an open sheet provides a template that promotes opening of the next MACPF domain to join the ring, thus propagating assembly. Comparisons with the 3 structurally-related classes of cytolysins, (Perforin, *Photorhabdus luminescens* (PLU) and the cholesterol dependent cytolysin, PFO) suggest that they adopt a remarkably similar 3-dimensional organization and regulatory mechanism, despite differences in the tertiary folds of the auxiliary domains and their location in the primary sequence (N- versus C-terminal to the MACPF domain). This similarity includes a special domain at the "base" of C6 that may mediate initial membrane attachment and position it at an optimal height for membrane insertion, as well as the domain that both locks the β-sheet in its closed conformation and the membrane-inserting elements in their pre-pore conformation.

Keywords: complement, immunology