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Autoinhibition and Activation of the Autolysin Auto from *Listeria Monocytogenes.* Lilia Polle[a], Maike Bublitz[a], Wolf-Dieter Schubert[a]. [a]*Molecular Host Pathogen Interactions, Division of Structural Biology, Helmholtz Centre for Infection Research, Braunschweig, Germany.*
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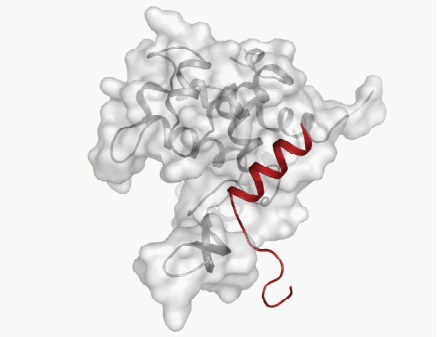
The opportunistic food-borne pathogen *Listeria monocytogenes* causes listeriosis in immuno-compromized humans. Virulence factors, crucial to the infection cycle, include an autolysin or cell-wall hydrolase Auto, not conserved in the related, non-pathogenic *L. innocua*. Auto is essential for efficient host cell invasion [1]. The link between a cell-wall modifying enzyme and bacterial pathogenesis however remained obscure. Our biochemical and functional analyses indicate that Auto is a highly efficient and tightly regulated enzyme with a role in coordinating the escape of the pathogen from the phagosome by regulating the porosity of the Gram-positive bacterial cell wall [2]. Its finely balanced features allow Auto to participate in infection but prevent uncontrolled cell lysis. These features include: i) its secretion as an inactive pro-enzyme ($Auto_{pro}$) proteolytically activated by a pH-controlled, dedicated protease; ii) its C-terminal GW-domains ensure its localization to the lipoteichoic acid molecules of the cell wall and limit its radius of activity; iii) activated Auto is an *N*-acetylglucosaminidase that preferentially hydrolyses acetylated peptidoglycan; iv) its acidic pH optimum ensures its enzymatic activity in the acidified phagosome but prevents inactivity once the phagosomal membrane has been breached.
The crystal structure of Auto reveals that i) it belongs to group 73 of glycosidic hydrolases, of which no structure was previously available and that ii) autoinhibition is achieved by an N-terminal α-helix physically blocking the substrate-binding cleft (Figure). A salt-bridge and hydrophobic interactions between the N-terminal α-helix and the substrate-binding cleft as well as the length of the loop connecting the α-helix to the catalytic domain are critical for optimal autoinhibition.



Crystal structure of autoinhibited autolysin Auto (white) with the inhibitory α-helix (red)

[1] Cabanes, D., Dussurget, O., Dehoux, P. und Cossart, P. **2004**. *Mol. Microbiol.* 51, 1601-1614. [2] Bublitz M, Polle L, Holland C, Heinz DW, Nimtz M, Schubert W-D. **2009**. *Mol. Microbiol.* 71, 1509-22.

Keywords: structural biology; bacterial pathogenesis; cell-wall hydrolase

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Structure of a Chicken MHC Class I Molecule with a Peptide-Devoid Binding Groove. Chee Seng, Hee[a], Song, Gao[b], Rolf Misselwitz[a], Marcia M. Miller[c], Ronald M. Goto[c], Andreas Ziegler[a], Oliver Daumke[b], Barbara Uchanska-Ziegler[a]. [a]*Charité-Universitätsmedizin Berlin, Institut für Immungenetik, Berlin, Germany.* [b]*Max-Delbrück-Centrum für Molekulare Medizin, Berlin, Germany.* [c]*Beckman Research Institute, Division of Molecular Biology, City of Hope, Duarte, United States.*
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*YF1*7.1* is an allele of a polymorphic major histocompatibility complex (MHC) class I locus within the chicken *Y* gene complex that harbours several MHC-like genes. The *Y* complex has been associated with allograft rejection and differential resistance to Marek's disease virus and Rous sarcoma virus infection. In this study, we aim to understand the possible role of the YF1*7.1 molecule in antigen presentation. The complex of YF1*7.1 heavy chain (HC) and chicken β_2-microglobulin, but without a peptide, was purified and crystallized in space group $P2_1$. It diffracted synchrotron radiation to 1.32 Å resolution and the structure was solved by molecular replacement using the peptide-stripped chicken BF2*2101 (PDB code 3bew) as search model. The YF1*7.1 structure is similar to BF2*2101, but possesses a narrower and more hydrophobic binding groove. Four out of eight highly conserved residues reported to be essential in sequence-independent anchoring of peptide antigens in classical class I molecules are substituted in YF1*7.1, leading to unprecedented interactions of HC atoms in the binding groove. A comparison with mammalian MHC class I structures, together with BF2*2101, revealed the existence of several avian-specific structural features of the HC due to sequence differences and deletions. Careful scrutiny of the electron density maps in the ligand binding groove shows no ordered or unbroken density comparable to that seen in classical class I molecules which display a peptide. The YF1*7.1 structure supports the previous prediction that, despite sharing many structural features with BF2*2101, YF1*7.1 is unlikely to bind antigen in the same manner as this classical MHC class I molecule. The structure also provides insights into the type of ligand that could be bound by the YF1*7.1 molecule, thereby suggesting a possible function.

Keywords: YF1*7.1; chicken Rfp-Y; MHC class I antigens