Structural insight into the mechanism of activation of the Toll receptor
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The Drosophila Toll receptor, which functions in both embryonic patterning and innate immunity to fungi and Gram-positive bacteria, is activated by a dimeric cytokine ligand, Spätzle (Spz). Previous studies have suggested that Spz crosslinks two Toll receptor molecules to form an activated complex. Here we report electron microscopy structures of the Toll ectodomain in absence and in presence of Spz. Contrary to expectations, Spz does not directly crosslink two Toll ectodomains. Instead Spz binding at the N-terminal end of Toll predominantly induces the formation of a 2:2 complex, with two sites of interaction between the ectodomain chains, one located near to the N-terminus of the solenoid, the other between the C-terminal juxtamembrane sequences. Moreover Toll undergoes a ligand-induced conformational change, becoming more tightly curved than in the apo form. The unexpected 2:2 complex was confirmed by mass spectrometry under native conditions. These results suggest that activation of Toll is an allosteric mechanism induced by an end-on binding mode of the ligand.

Keywords: Toll receptor, electron microscopy structures, ligand binding

Electrostatic potential analysis of the ferroelectric phases of perovskite oxides using CBED
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We have been developing a method to refine crystal structural parameters using convergent-beam electron diffraction (CBED), which can determine atom positions, Debye-Waller factors (atomic displacement parameters) and low-order structure factors from a nanometer-size area of specimens. The electrostatic potential and electron density distributions are reconstructed from the refined parameters. Especially for the determination of electrostatic potential, CBED is more advantageous than the X-ray method because the Fourier coefficients of electrostatic potential are directly determined and the electrostatic potential is reconstructed without any errors caused by the conversion of structure factors. The electrostatic potential consists of the positive contribution from nuclear charge and the negative one from electrons. The behaviors of valence electrons alter the balance between the contributions of nuclear charge and electrons, which may cause large changes in the electrostatic potential. We have applied the method to the ferroelectric phases of perovskite oxides such as BaTiO$_3$ and PbTiO$_3$. Energy-filtered CBED patterns were obtained from a single domain regardless of the existence of complicated ferroelectric domains. The direction of ferroelectric polarization can be readily identified from the CBED patterns due to the strong dynamical diffraction effect. Electronic polarizations of the atoms have been observed through electrostatic potential gradients, which are caused by relative shifts between the nuclear charge and electrons.


Keywords: electrostatic potential, convergent-beam electron diffraction, ferroelectrics

Differential diffraction
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Keywords: differential, diffraction, electron microsopy

Observed in leukocyte beta(2) integrins, alpha(X)beta(2) and alpha(L) beta(2). However, 24 kinds of integrin heterodimers exhibit their own unique ligand-binding activities and function. Unlike the integrins existing in platelets or blood corpuscles including alpha(IIb)beta(3), alpha(V)beta(3), alpha(X)beta(2), alpha(L)beta(2) and so on, integrin alpha(3)beta(1), alpha(6)beta(1), alpha(7)beta(1) and alpha(6) beta(4) constantly bind to their ligands, laminins at the basement membrane. Therefore, we focused on the laminin-binding integrins and determined the structures by the electron microscopy to address the ligand specific integrin-ligand binding mechanism.

Keywords: electron microscopy, cell adhesion, structural biological function