Structure Helps Yield Drug "Hypersensitivity" Tests for Patients

Scientific Achievement

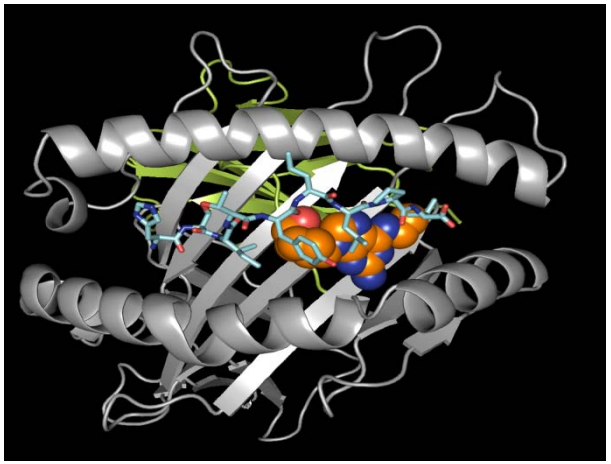
X-rays used to solve the structure of the HIV/AIDS antiviral drug abacavir bound to an immune system-related gene, thus showing how the drug triggers the immune response

Significance and Impact

The structure helped researchers develop tests for drug "hypersensitivity," a potentially fatal over-reaction of the immune system, before a patient takes it

Research Details

- X-ray crystallography used to determine the structure of a molecule complex consisting of a peptide (a short protein) bound to protein produced by the gene "HLA-B*57:01" in the presence of abacavir
- Structure shows that abacavir attaches to the HLA-B*57:01 protein's "binding groove" and also weakly bonds to the peptide and the gene, causing the gene to present unknown peptides to white blood cells
- Having never seen the peptides before, the cells treat them as foreign and launch an aggressive immune attack



Abacavir (orange, blue, and red spheres) interacting with the HLA-B*5701 protein (gray), causing the protein to "show" the immune system a peptide it has never seen (light blue). The immune system assumes it is foreign and attacks, resulting in drug hypersensitivity.

D Ostrov, B Grant, Y Pompeu, J Sidney, M Harndahl, S Southwood, C Oseroff, S Lu, J Jakoncic, C de Oliveira, L Yang, H Mei, L Shi, J Shabanowitz, AM English, A Wriston, A Lucas, E Phillips, S Mallal, H Grey, A Sette, D Hunt, S Buus, B Peters, *Proc Natl Acad Sci USA* 109:9959-9964 (2012)

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