Crystal Structure of OXA-24, a Novel Class D β-lactamase with Carbapemenase Activity

Elena Santillana[a], Germán Bou[b], Antonio Romero[a], [a]*Centro de Investigaciones Biológicas, CSIC, Ramiro de Maeztu, 9, 28040-Madrid (Spain).* [b]*Complejo hospitalario universitario Juan Canalejo; A Coruña (Spain).* E-mail: esh@cib.csic.es

One of the main concerns in Medicine is the presence of microorganisms causing infections which harbour antibiotic resistance mechanisms. Among the different mechanisms associated with antibiotic resistance, much attention is currently being focused on the presence of β-lactamases. Oxacillinases are Ambler class D β-lactamases that possess active site serine groups like class A and class C β-lactamases. These enzymes are characterized by their hydrolytic activity for isoxazolyl, penicillins, methicillin and aztreonan significantly, sparing most extended-spectrum cephalosporins.

Six oxacillinases with carbapenem-hydrolyzing activity have been sequenced from *Acinetobacter baumannii*. OXA-24 shares 40% identity with a group of oxacillinases consisting of OXA-5, -7, -10 and -11. Despite these similarities, some interesting and differing features exist between previous oxacillinases and OXA-24. Thus, OXA-24 lacks hydrolytic activity against oxacillin, cloxacillin, and methicillin but displays a moderate level of resistance to carbapenemes. Crystals of OXA-24 from *A. baumannii* were grown using the vapour diffusion technique. They belong to space group $P4_12_12$, with cell dimensions a=b=102.2 Å, c=86.1 Å and one molecule in the asymmetric unit, which diffracted beyond 2.5 Å. It was possible to locate the position of the enzyme in the unit cell using molecular replacement with the coordinates of OXA-10 as a search model. The three dimensional structure of OXA-24 could establish the molecular basis to explain the relevance of the substitutions in its hydrolytic activity. The structure is currently undergoing refinement.

Keywords: β-lactamases, antibiotic resistance, protein crystallography