Annexin III is the only member of the annexin family for which an enzymatic activity has been proposed: it was identified as an inositol 1,2-cyclic phosphate 2-phosphohydrolase (1).

Annexins are a family of calcium and phospholipid binding proteins whose biological function is not well defined yet. They consist of a highly conserved C-terminal core of four (exceptionally eight) repeats of about 70 amino acids, and a more variable N-terminus (2). Unlike most members of the family, annexin III is expressed preferentially in neutrophiles, in their final stage of differentiation (3). The 3D structure of the conserved core of annexins V and I shows a protein formed of 4 structural domains, with a hydrophilic channel between modules formed of domains 1+4 and 2+3. The calcium binding sites are all located on one side of the molecule that has thus been defined as the membrane-binding surface.

The overall structure of annexin III is similar to that of annexin V, but with a well defined calcium site in domain 3, which is observed only under high calcium conditions for annexin V. The N-terminus of annexin III carries a Trp which lies with its side-chain inserted into the hydrophilic space between the modules described above, which may affect any potential ion channel activity. The relative position of domain 3 with respect to domain 2 is different from annexins I and V, suggesting a molecular flexibility that may be important for the attachment of annexins on membrane surfaces (4).

The crystals grown in the presence of inositol-1,2-phosphate (InP) are not isomorphous to native ones, yet we find only one molecule of InP in the structure. It lies on the calcium-binding surface of the protein, interacting with a secondary calcium site in domain 3. The presence of its charged phosphate group favours the coordination of a further metal ion on this surface. Its location does not suggest an enzyme active site, but on the basis of its presence on the membrane-binding surface of annexin we can model the interaction of annexins with phospholipids embedded in a membrane.

The crystal structure of an acidic scorpion neurotoxin BmK M8 has been determined by using molecular replacement method. It is the first acidic α-scorpion neurotoxin reported so far. Compared with the basic and most potent α-toxin, AaH II, the BmK M8 is a relatively inactive toxin (1100 times less active than AaH II) with an unusually low isoelectric point (5.3). The much drop in toxin lethality is accompanying the acidic property of the molecule. The refined structure showed new functionally important area and some features of the toxin-receptor binding. In association with the information from antibody mapping for localization of binding site on sodium channel, a multiposition mode for the toxin-receptor interaction and three "toxic regions" related to the binding process, including Face A, Face B and Site C are proposed. The Face A, mainly consists of Tyr5, 35, 47, α-amino group, Arg2 and Asp3, may be more essential for the binding; the Face B, mainly comprised conserved residues Tyr14, 21, Lys28 and Val55, may contribute to the high efficacy of the binding process and substitutions of acidic residues in this area will strongly weaken the toxic activity; and the Site C formed by Lys58 and Arg62 from C-terminal and Arg41 and Tyr42 from loop 38-44 may be involved in the binding sitespecificity. On basis of these, a toxin-sodium channel binding model will be proposed.

BmK M8 was purified from Chinese scorpion Buthus martensi Karsch. The crystals of BmK M8 belong to space group P2₁ and contains one molecule per asymmetric unit. The structure model of BmK M8 has been refined to a R factor of 18.1% with data from 8Å to 1.85Å.