

MS11-2-2 C-type lectin-(like) fold interaction patterns in protein:protein complex formation
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Abstract

C-type lectins are carbohydrate-binding proteins which utilize calcium for the carbohydrate binding. The fold typically consists of two α -helices, two small β -sheets and a long surface loop, with two or three disulfide bridges. C-type lectin-like (CTL) proteins are proteins of the same fold, not necessarily containing calcium or binding carbohydrates, with miscellaneous functions in organisms and often forming protein:protein complexes. Recently, we have solved the structure of a CTL:CTL complex, human natural killer cell receptor NKR-P1 in complex with its ligand LLT1 ([1], PDB code 5MGT). This opened for us the question of general principles of CTL:protein complex formation.

In order to get a more complex view, the PDB database has been scanned and 77 structurally known CTL:protein complexes have been found [2]. There are complexes of CTL snake venom proteins, NK receptor complexes, complexes with immunoglobulin, intimin:TIR complexes, complexes of Epstein-Barr virus gp42 glycoprotein, lectican:tenascin complex and complex of artificial binder, TNFalpha antagonist. Moreover, CTL proteins often act as homodimers (NK receptors) or heterodimers (snake venom proteins, NK receptors, SPL-1 protein). To compare the mutual positions of binding partners in the complexes, all CTL partners were superimposed to selected CTL protein, CD69 (PDB code 3HUP). Complex-forming residues were denoted by colour on the surface of CD69.

It was found that CTL:protein binding varies in its form and strength, from picomolar to milimolar K_D and with various interaction interfaces. In projection to CD69, nearly all surface is covered by contact residues in CTL:protein complexes (heterodimers included). When heterodimeric contacts are excluded, still a large part of the surface is covered. However, when the frequency of residue usage in interactions is highlighted, "canonical" binding clearly predominates (Fig. 1).

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References

- [1] Blaha, J., Skalova, T., Kalouskova, B., Skorepa, O., Cmunt, D., Pazicky, S., Polachova, E., Abreu, C., Stransky, J., Koval, T., Duskova, J., Zhao, Y., Harlos, K., Hasek, J., Dohnalek, J., Vanek, O., 2021. Crystal structure of the human NKR-P1 bound to its lymphocyte ligand LLT1 reveals receptor clustering in the immune synapse (preprint). bioRxiv 2021.06.16.448687. <https://doi.org/10.1101/2021.06.16.448687>.
- [2] Dohnalek, J., Skalova, T. C-type lectin-(like) fold – Protein-protein interaction patterns and utilization, *Biotechnology Advances*, in press, <https://doi.org/10.1016/j.biotechadv.2022.107944>

Interactions mapped on CD69. Taken from [2].

