MS11-P04

The crystal structure of the CARD-CARD disk of the human apoptosome and its structural insights into the assembly of the death-domain fold

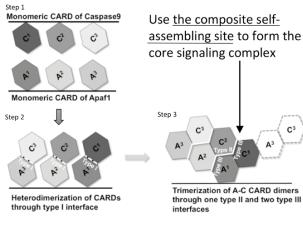
Su-Chang Lin¹, Yu-Chih Lo², Tsung-Wei Su¹

- 1. Genomics Research Center, Academia Sinica, Taipei, Taiwan
- 2. Department of Biotechnology and Bioindustry Sciences, National Cheng Kung University, Taipei, Taiwan

email: tomlin@gate.sinica.edu.tw

The caspase recruitment domain (CARD) of the human apoptosome recruits caspase-9 CARD via the homotypic interactions for caspase activation in apoptosis. Here we present the crystal structure of the CARD-CARD disk of the human apoptosome and also show the difference in the CARD assembly between the *Caenorhabditis elegans*, Drosophila, and human apoptosomes, which suggests that the helical assembly only exists in the vertabtate DD-folds. We also found that of the death-domain folds have five different assembling mechanisms for their specific roles in signal transduction.

The CARD-CARD disk of the human apoptosome



References:

- [1] Su, TW et. al. (2017). Structure, 25, 407-420.
- [2] Kao WP et. al. (2015) Apoptosis. 20. 174-195

Keywords: Apoptosome, assembly, death domain

MS11-P05

Structure of human natural killer cell receptor NKR-P1 in complex with its ligand LLT1

Tereza Skalova¹, Jan Bláha², Jan Stránský¹, Tomáš Kova¹, Jarmila Dušková¹, Yuguang Zhao³, Karl Harlos³, Ondřej Vaněk², Jan Dohnálek¹

- 1. Institute of Biotechnology CAS, The Czech Academy of Sciences, v.v.i., Průmyslová 595, 252 50 Vestec, Czech Republic
- 2. Department of Biochemistry, Faculty of Science, Charles University, Hlavova 8, 128 40 Prague, Czech Republic
- Division of Structural Biology, The Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, OXFORD OX3 7BN, United Kingdom

email: t.skalova@gmail.com

Natural killer cells are white blood cells able to kill tumor, virus-infected or stressed cells. NKR-P1 is a C-type lectin like-receptor on surface of human natural killer cells and LLT1 is its binding partner belonging to the same structural family.

Recently, we have expressed, purified and solved four crystal structures of the extracellular part of LLT1 in monomeric, dimeric and hexameric form [1, 2]. In this contribution, we present three more structures characterizing this receptor-ligand binding pair: structures of the extracellular part of NKR-P1 in the fully glycosylated and deglycosylated form and a structure of the NKR-P1:LLT1 complex. Expression and purification of NKR-P1 was described by us recently as well [3].

All three crystal structures show NKR-P1 in a dimeric form with an unexpected dimerization mode. Unlike LLT1, which has the α 2 helix in the dimerization interface, NKR-P1 dimer has the α 1 helix in its dimerization interface. This different dimeric arrangement of both proteins enables spatial connection of NKR-P1 with LLT1 not only in a single molecular complex, but in a periodical chain of alternating receptor/ligand molecules. Such chain we really observe in the presented crystal structure.

Acknowledgement: This study was supported by BIOCEV (ERDF CZ.1.05/1.1.00/02.0109), Czech Science Foundation (15-15181S and 18-10687S), MEYS of the Czech Republic (LTC17065 within the COST Action CA15126), Charles University (UNCE 204025/2012, GAUK 161216), and Instruct (R&D pilot scheme APPID 56 and 286).

References:

Bláha, J. et al (2015). Protein Expr. Purif. 109, 7-13
Skálová, T. et al (2015). Acta Cryst. D71, 578-591
Bláha, J. et al (2017). Protein Expr. Purif. 140, 36-43

Keywords: immune receptor, natural killer cell, protein-protein complex