The Structure of USP7 at Ambient Temperature by Using X-ray Crystallography

Nowadays cancer is a serious problem that doesn't have very efficient treatment approaches. According to the world health organization (WHO) 10 million people died because of cancer in 2020. [1] Some mutations in DNA cause cancer and these cancer cells hide from cell cycle regulators and avoid cell death called apoptosis by using many methods. However, once cancer cells can undergo apoptosis and prevent tumor development, cancer processes can get slower or regress. P53 is a very crucial gene to control the cell cycle and apoptosis mechanism. Ubiquitination of P53 lead to its degradation.[1][2][3][4] The decrease in the level of p53 expression in the cell due to the degradation, and apoptosis decreases in direct proportion. P53 has a regulatory relationship with USP7 protein (Ubiquitin-specific-processing protease 7). USP7 mainly functions about deubiquitinating like deubiquitinating the P53. In other words, USP7 help to increase in P53 expression level and reduce cancer development. Researchers show how usp7 is important for cancer treatment.[2][3][4] To better understand usp7 and its functions, we need to observe its ambient structure. According to achieve this structure, USP7 protein expression was obtained at 18 ℃ with 5uL 0.4M IPTG per 150 mL. Then we going to crystalize them with 3500 different commercial conditions and check their structure with Turkish DeLight. [5] Turkish DeLight is a very important X-ray crystallography device which is sending the X-ray photons through the crystal plate and collecting the diffraction data with a detector from behind the crystal plate for 1 min and 45 sec (5 secs/frame) while oscillation occurs. Finally, data will be processed with CrysAlisPro, and the structure determined with Phenix and COOT. On the other hand, using x-ray crystallography has a significant disadvantage. X-ray photons cause radiation damage which affects the protein structure. [5]

References:

[1] Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Global Cancer Observatory: Cancer Today. Lyon: International Agency for Research on Cancer; 2020 (https://gco.iarc.fr/today, accessed February 2021).

[2] Qi SM, Cheng G, Cheng XD, Xu Z, Xu B, Zhang WD, Qin JJ. Targeting USP7-Mediated Deubiquitination of MDM2/MDMX-p53 Pathway for Cancer Therapy: Are We There Yet? Front Cell Dev Biol. 2020 Apr 2;8:233. doi: 10.3389/fcell.2020.00233. PMID: 32300595; PMCID: PMC7142254.

[3] Wang Z, Kang W, You Y, Pang J, Ren H, Suo Z, Liu H, Zheng Y. USP7: Novel Drug Target in Cancer Therapy. Front Pharmacol. 2019 Apr 30;10:427. doi: 10.3389/fphar.2019.00427. PMID: 31114498; PMCID: PMC6502913.

[4] O'Dowd CR, Helm MD, Rountree JSS, Flasz JT, Arkoudis E, Miel H, Hewitt PR, Jordan L, Barker O, Hughes C, Rozycka E, Cassidy E, McClelland K, Odrzywol E, Page N, Feutren-Burton S, Dvorkin S, Gavory G, Harrison T. Identification and Structure-Guided Development of Pyrimidinone Based USP7 Inhibitors. ACS Med Chem Lett. 2018 Feb 21;9(3):238-243. doi: 10.1021/acsmedchemlett.7b00512. PMID: 29541367; PMCID: PMC5846043.

[5] Gul, M., Ayan, E., Destan, E., Johnson, J., Shafiei, A., Kepceoglu, A., Yilmaz, M., Ertem, F., Yapici, ., Tosun, B., Baldir, N., Tokay, N., Nergiz, Z., Karakadio glu, G., Paydos, S., Kulakman, C., Ferah, C., Güven, ., Atalay, N., Akcan, E., Cetinok, H., Arslan, N., \c Sabano\u glu, K., A\c sci, B., Tavli, S., Gümüsbo\u ga, H., Altunta\c s, S., Otsuka, M., Fujita, M., Tekin, ., \c Cift\c ci, H., Durda\u gi, S., Karaca, E., Kaplan Türköz, B., Kabasakal, B., Kati, A., & DeMirci, H. (2022). Rapid and High-Resolution Ambient Temperature Structure Determination at Turkish Light Source. bioRxiv.