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## **Protein-Protein Interactions between Interleukin-18 and Interleukin-19 in Diabetic Nephropathy Based on Bioinformatics Study**

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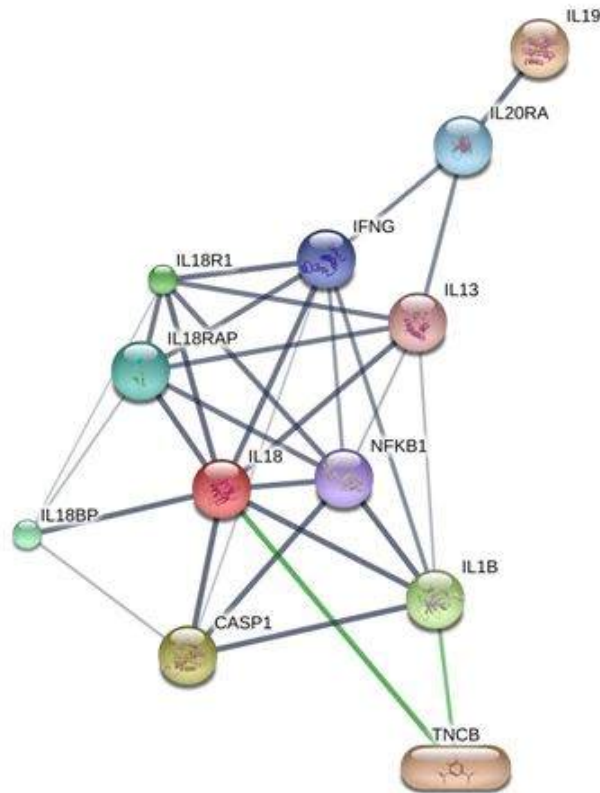
**Objectives:** Diabetes mellitus (DM) is a chronic metabolic disease marked by hyperglycemia and the complication of DM can cause diabetic nephropathy (DN). Some evidences showed that DN was mediated by several inflammatory cytokines. IL-18 is one of potent inflammatory cytokines driving progression of DN. IL-18 has ability to induce IL-1, TNF- $\alpha$ , and IFN- $\gamma$  production in DN. Elevated expression of IL-18 is consistently found in serum and urine of DN patients. A recent report uncovered the level of IL-19 has a strong positive correlation with urinary albumin excretion rate (UAE) and Cystatin-C in DN patients and IL-19 may be one of key players in DN. Although IL-18 and IL-19 are considered to be involved in the progress of DN, however there is no report about their molecular interaction. This study aimed to uncover molecular interaction between IL-18 and IL-19 in DN.

**Methods:** The prediction of molecular interaction between IL-18 and IL-19 was done by using STITCH bioinformatics software v.5.0. "IL18" and "IL19" were set as keywords used for bioinformatics analysis and to predict protein-protein interactions in human, *Homo sapiens* was selected. After reviewing variant of molecules based on keywords used, STITCH generated prediction of biological pathway between IL-18 and IL-19.

**Results:** Based on this bioinformatics study, IL-18 and IL-19 were associated with IL-13 and IFN- $\gamma$  activity. Activation of IL-20RA by IL-19 led to modulation of IL-13 and IFN- $\gamma$  expression. This result also showed that IL-18 had ability to regulate the expression of IL-13 and IFN- $\gamma$ .

**Conclusions:** It can be concluded that the activation of both IL-18 and IL-19 may synergistically regulate IL-13 and IFN- $\gamma$  expression. However, the laboratory-based research should be done to prove this prediction.

Figure 1. Prediction of protein-protein interactions between IL-18 and IL-19



**Molecular prediction of protein-protein interactions between IL-18 and IL-19 in DN.** “IL18” and “IL19” were used to conduct STITCH analysis. This biological pathway shows 10 interactors related to IL-18 and IL-19. This bioinformatics analysis was done on Monday, February 17, 2020 at 9.00 PM.