Homology Modeling and *in Silico* Exploration of Functional Domain of Interleukin-27 for New Drug Leads in the Management of Type-1 Diabetes

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Abstract—*Type 1 diabetes (T1D) is an autoimmune disease. It is due to the selective destruction of insulin-producing pancreatic beta cells. IL-27 plays key role in the regulation of these cells through Th-17 and Th-1. Here, IL-27 is involved in the production of Th1 cells which promote the secretion of IFN-γ ultimately leading to the destruction of Pancreatic Beta cells. It is also involved in the deactivation of Th17 cells leading to the enhanced levels of pancreatic beta cells. Hence, IL-27 may be a good target to modulate the levels of pancreatic beta cells and thereby to address the T1D. However, the crystal structure of IL-27 is thus far not reported. In this backdrop, as the crystal structure of IL-27 is not available, its homology model has been developed through Modeller by using 1CNT as template structure. The developed model showed satisfactory stereo-chemical quality scores which include Ramachandran plot (93.6%), Errat plot (82.632) and Prosa plot (-2.67). An analysis of the IL-27 model in DogSite Server indicated the possibility of eleven pockets to accommodate the prospective ligands. Among these, the pocket P0 with 13 residues (simple score- 0.49) has been adopted as ligand binding domain to modulate the activity of IL-27. Considering the autoimmune nature of T1D, Ustekinumab considered as prospective scaffold for modulating IL-27. Molecular docking was carried out against P0 target of IL-27 with Ustekinumab in Dockblaster to identify other prospective modulators. This has resulted in identifying several compounds for modulating IL-27. Among these ZINC39962616 (N,N-dimethyl-2-oxo-benzimidazole-5-sulfonamide) showed best Dock score (-61.77). The study opened avenues for the synthesis and biological evaluation of this class as prospective T1D agents.*