NOVEL TARGET IDENTIFICATION AND DRUG REPURPOSING FOR SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS (sJIA): AN *INSILICO* APPROACH

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INTRODUCTION:

- Systemic Onset Juvenile Idiopathic Arthritis (sJIA) is the rarest form of juvenile idiopathic arthritis (JIA) associated with dysregulation of innate immune system. IL-1 and IL-6 play a major role in the pathogenesis of sJIA.
- It is characterized by fever, lymphadenopathy, arthritis, rash, and serositis. Severe complications involving growth delay, bone and cartilage erosion with functional handicap, and a risk of osteopaenia continue to be a major concern.
- This study aims to identify novel potential druggable targets and determine the off-label therapeutic possibilities for sJIA.

METHODOLOGY:

- Differentially Expressed Genes (DEGs) were retrieved from GSE103500 of GEO database through GEO2R.
- The Protein Protein Interactions (PPI) of existing genes from NCBI and DEGs obtained from GEO2R were studied using STRING.
- Genes having direct interaction with the known genes were selected. Drugs for the selected targets were gathered from Drug Repurposing Hub, NIH LINCS project.
- Drug similarity search for the standards were performed in DrugBank.
- Standards and similar drugs were docked using Schrodinger Glide tool with the target obtained from PDB.
- Pharmacokinetic and physiochemical properties were predicted using Qikprop analysis.

RESULT:

- A total of 429 genes (P<0.05, logFC>2) including both up and down regulated genes were obtained.
- PPI analysis revealed membrane metallo-endopeptidase (MME) with significant interactions which was an upregulated gene.
- Sacubitril and racecadotril having 6 and 7 similar drugs respectively were obtained as standard inhibitors for MME. Sacubitril, sacubitrilat, Methylphenidate and dexamethylphenidate were found to have better docking score and obeyed Lipinski's rule of five.

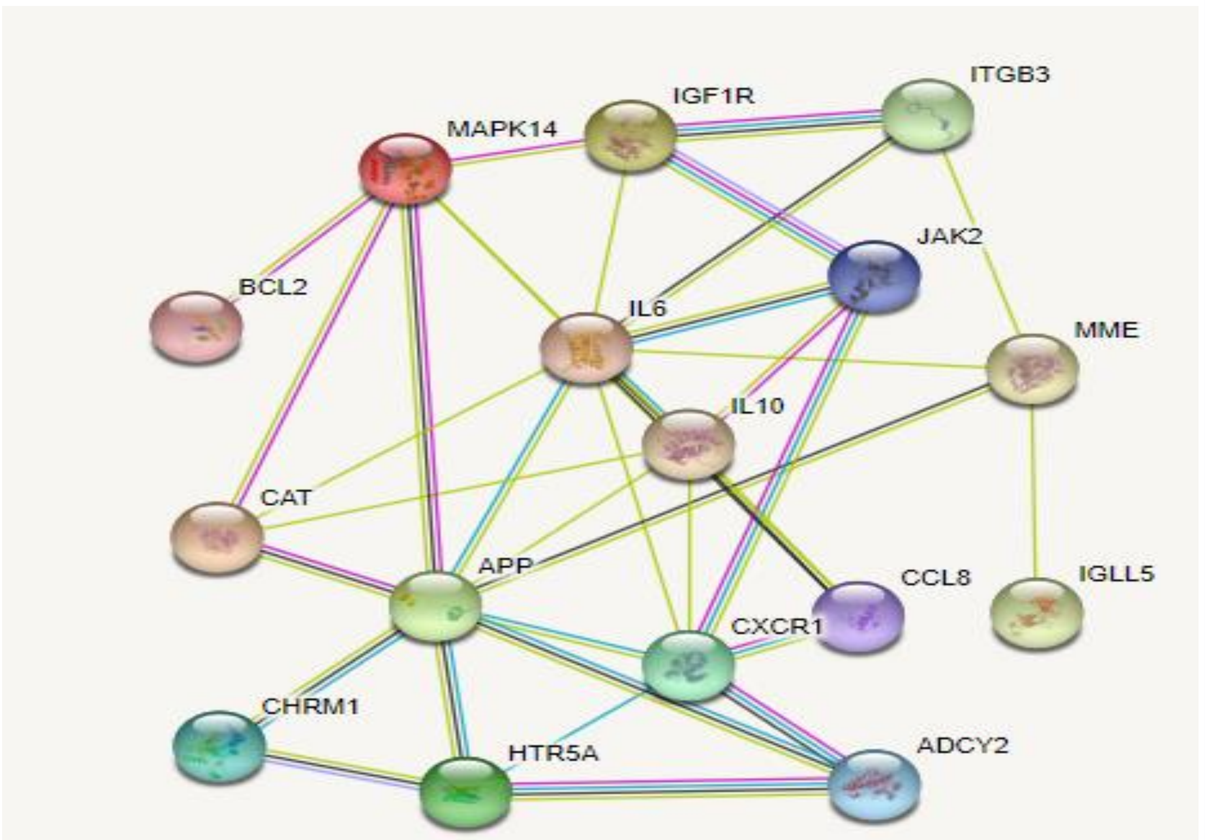

Fig.1: PPI of existing and DEGs

Table. 1: docking scores of drugs targeting MME

Drug Name	Docking Score	Glide Energy	Lipinski's rule of five
Sacubitrilat	-14.953	-72.057	1
Sacubitril	-11.953	-67.863	0
Methylphenidate	-4.178	-29.284	0
dexmethylphenidate	-4.178	-29.284	0

CONCLUSION:

- Exploring key pathogenic factors and drug re-appraisal would circumvent initial stages of drug discovery.
- Therefore, these hypothesis serve as an excellent basis for further *invitro* and *invivo* studies suggesting that Sacubitril, Sacubitrilat, Methylphenidate and Dexamethylphenidate drugs could be repurposed for sJIA.

REFERENCES:

1. Woo, P., 2006. Systemic juvenile idiopathic arthritis: diagnosis, management, and outcome. *Nature clinical practice rheumatology*, *2*(1), pp.28-34.
2. Martini, A., 2012. Systemic juvenile idiopathic arthritis. *Autoimmunity reviews*, *12*(1), pp.56-59.

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