IN-SILICO DETERMINATION OF THERAPEUTIC POSSIBILITIES FOR TYPE-1 GAUCHER DISEASE: A GENE DATABASE LINKED ANALYSIS

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INTRODUCTION:

- Gaucher Disease (GD, OMIM #230800, ORPHA355) is a rare, autosomal, recessive genetic disease caused by mutations in the *GBA1* gene, located on chromosome 1 (1q21).
- This leads to a markedly decreased activity of the lysosomal enzyme, glucocerebrosidase (GCase, also called glucosylceramidase or acid β-glucosidase, EC: 4.2.1.25), which hydrolyzesglucosylceramide (GlcCer) into ceramide and glucose.
- Three clinical forms have been identified: type 1 is the most common and typically causes no neurological damage, whereas types 2 and 3 are characterized by neurological impairment.
- This study aimed to screen bio-targets of Type-1 Gaucher Disease (GD1, ORPHA77259) and to identify related drug molecules.

METHODOLOGY:

- The dataset GSE15568 included the gene expression profile of 5 GD1 and 4 controls, was downloaded from Gene Expression Omnibus (GEO) database.
- Differentially expressed genes (DEGs) were screened out using GEO2R.
- Hierarchical clustering and differences between the groups analysis were conducted for confirming these DEGs.
- Protein-Protein Interactions (PPI) was constructed using STRING.
- The DEGs were then entered into the Drug Repurposing Hub and DrugBank and related drug molecules were retrieved.

RESULTS:

- The genes linked with GD1 were found to be GBA, JAK2, MAPK14, DHX9, STAT1, IL1R1, CD44, EML4, IL6ST, FN1, EEA1, HBP1 and MCL1.
- The drugs with possibility of therapeutic repurposing, targeting these genes were found to be Anakinra, Hyaluronic acid, Bivatuzumab, Lanoteplase, Ocriplasmin and CKD-712

CONCLUSIONS:

- Drug repurposing is an unconventional drug discovery approach to explore new therapeutic benefits of existing, shelved and the drugs.
- Computational techniques circumvent expensive initial drug discovery phases and contemporary repurposing tools offer new molecular mechanisms of existing drugs.
- GD1 can often limit quality of life and is often associated with considerable morbidity. Therapeutic options for the same are limited which poses a threat to the lives of these patients. Drug repurposing proposes a new window of hope which could help make their lives better.

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