**REVEALING POTENTIAL MECHANISMS FOR EHLERS DANLOS SYNDROME USING KNOWLEDGE GRAPHS**

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Ehlers Danlos Syndrome (EDS) is a heritable connective tissue disorder with 14 subtypes. This investigation focuses on the hypermobile subtype (hEDS). hEDS presents as various symptoms and medical problems such as cardiological, neurological and gastrointestinal disorders. hEDS represents 80-90% of EDS cases and is thought to affect 1 in 5000 people worldwide . Despite its prevalence, there is not one known gene association or underlying mechanism. The lack of knowledge makes diagnosis and treatment difficult.

We used knowledge graphs (KGs) to interrogate the underlying mechanisms of hEDS. KGs combine heterogeneous, pre-existing data to represent relationships of interest. We used these relationships to explore potential hypotheses for the mechanism of action of hEDS, and worked with a clinical geneticist to evaluate the results.

We interrogated the Monarch KG, which contains information about genes, phenotypes, diseases, and their relationships, with a set of previously identified hEDS genes of interest, and expanded the list to include mouse orthologs. We then assessed phenotypes associated with hEDS to identify new phenotypically similar genes using semantic similarity algorithms. We focused on genes not already associated with hEDS or other subtypes. Two genes returned were LOX and ATP7A; both related to copper metabolism. Notably, heterozygous LOX mutations were found by the clinical geneticist in two patients with hEDS. Mutations in both genes have phenotypes often seen in hEDS patients, indicating copper metabolism should be further explored in trying to determine the underlying causes of hEDS.