

## Developing a community-driven knowledge based molecular pathway for Malignant Pleural Mesothelioma

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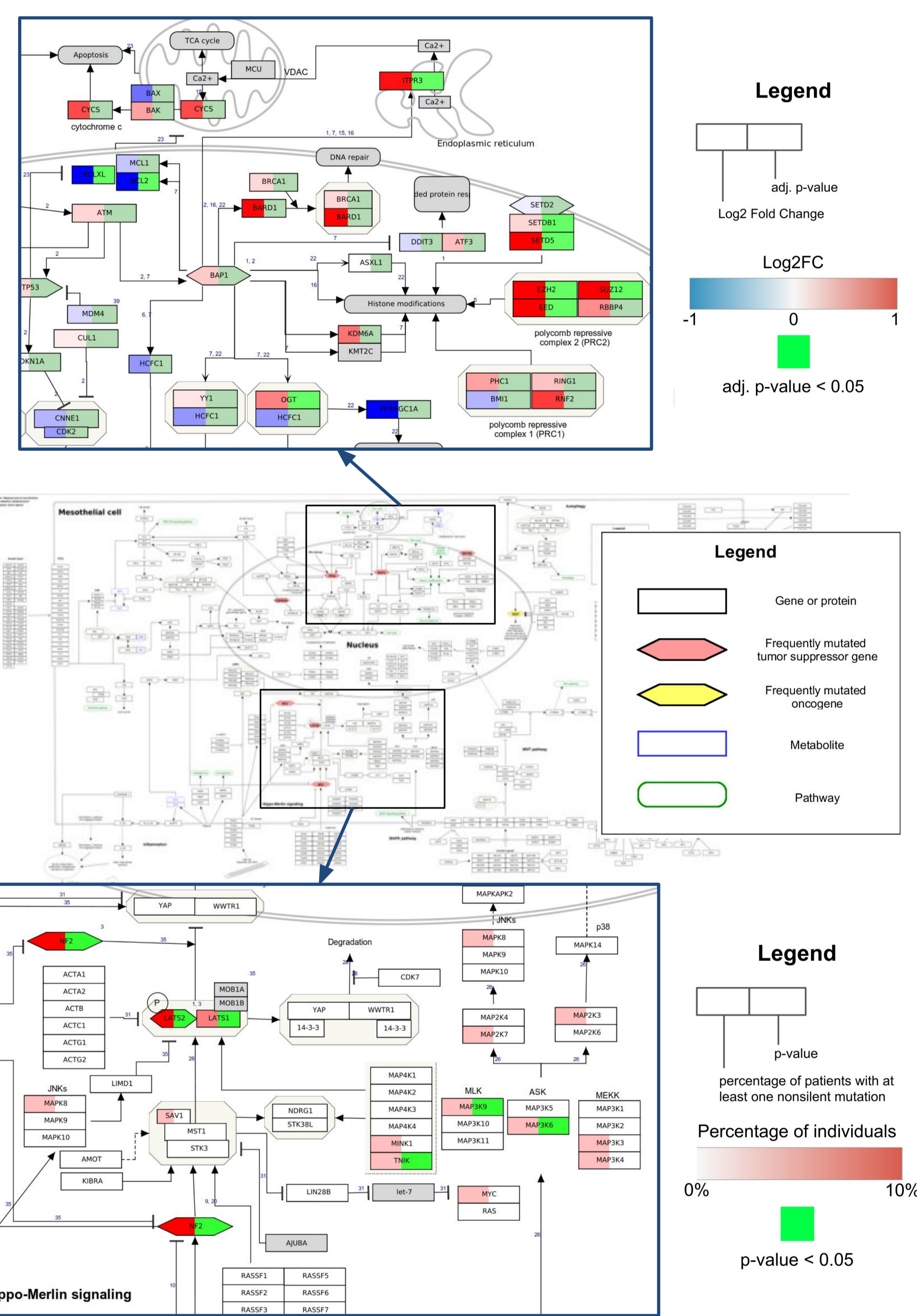
### Introduction

Our goal is to establish an openly accessible and interactive knowledge base platform on the molecular pathways relevant to pleural mesothelioma (PM) for research in biology, translational, and clinical fields. We have developed a molecular pathway for PM within the WikiPathways<sup>1</sup> database using PathVisio<sup>2</sup>, by curating papers from PubMed (2015 onwards)<sup>3</sup>. The current version of the PM molecular pathway model includes 455 genes/gene products, thirteen pathways, fourteen metabolites, and 247 unique interactions. The PM molecular pathway model serves as an open-access resource that integrates systems biology-oriented knowledge and statistics. It is a dynamic model that undergoes constant curation and expansion, allowing the active participation of the community in enhancing our understanding of PM at the molecular level. The pathway is accessible on [wikipathways.org/pathways/WP5087](http://wikipathways.org/pathways/WP5087).

### How to use

The PM molecular pathway model serves as an information source, and facilitates data analysis and interpretation across genomic, transcriptomic, and proteomic studies, enabling insights into the underlying molecular mechanisms of pleural mesothelioma. Its application spans toxicology, disease research, patient studies, and pharmaceutical investigations, aiding in the identification of genetic alterations, biomarkers, therapeutic targets, and drug development. The capabilities of data visualization of the molecular pathway are shown with two examples in **Figure 1**, showing data comparing gene expression in MPM to normal pleura (top) and nonsilent mutation frequency in patients (bottom).

The PM molecular pathway model harnesses the FAIR (Findable, Accessible, Interoperable, Reusable) principles of WikiPathways and other life sciences databases like neXtProt<sup>4</sup>, facilitating seamless integration of captured information across these resources. Two illustrative examples are showcased, where the power of SPARQL queries is employed to extract comprehensive details from WikiPathways (**Figure 2**) and neXtProt (**Figure 3**), enhancing the depth and breadth of information available for analysis and interpretation.

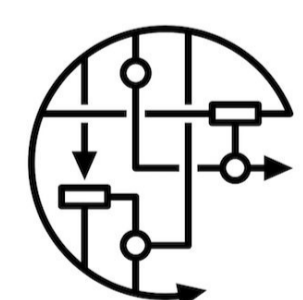


SPARQL Query:

```
1 select distinct ((substr(str(?hgnc),37) as ?hgnclabel) ?geneProduct ?entrez where {
2 ?geneProduct a wp:GeneProduct ; rdfs:label ?label ; dcterms:isPartOf ?pathway ;
3 wp:dbEntrezGene ?entrez ; wp:dbHgncSymbol ?hgnc .
4 ?pathway a wp:Pathway ; dcterms:identifier "WP5087" .
5 }
```

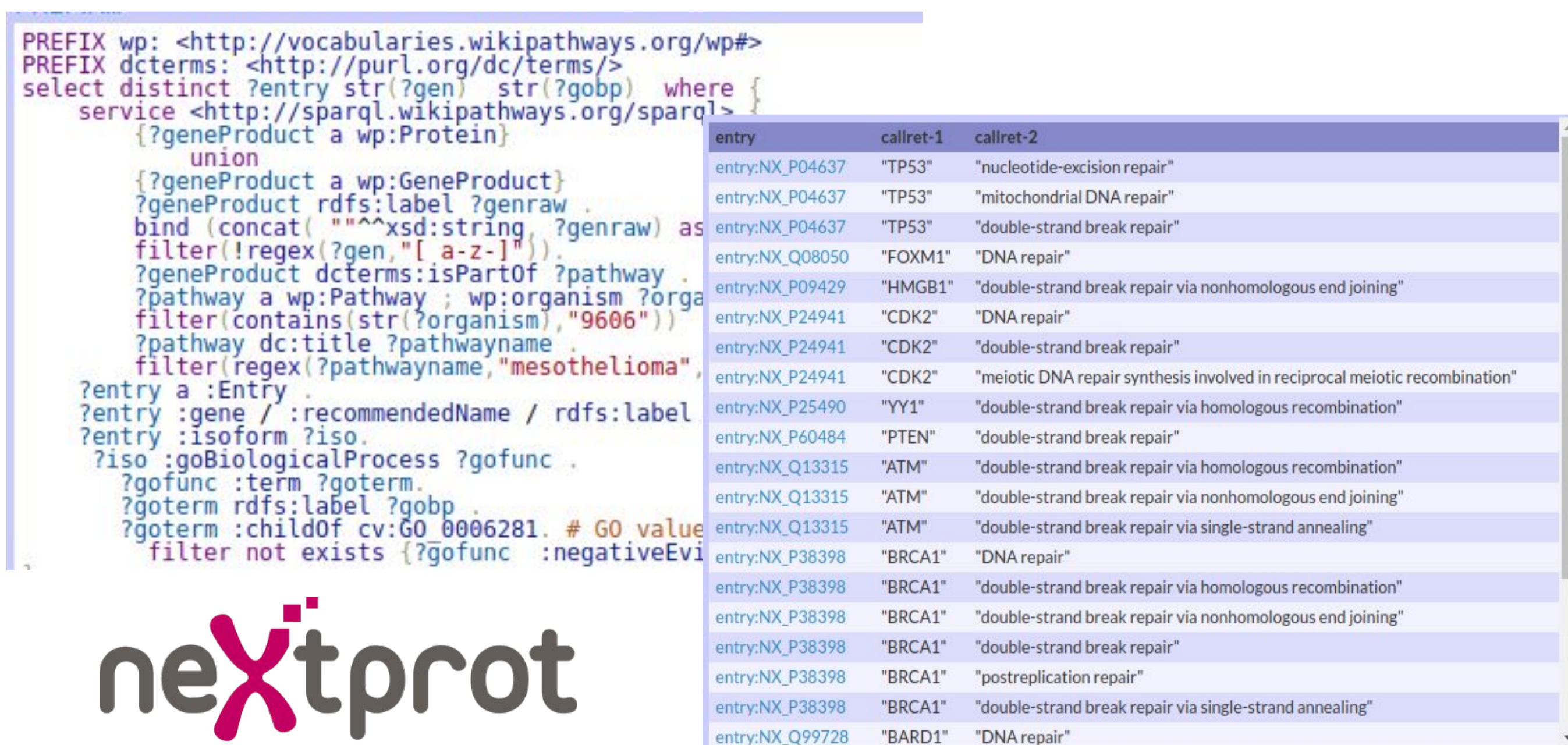
SPARQL results (441 results)

hgnclabel	geneProduct	entrez
EIF4G1	<a href="https://identifiers.org/ensembl/ENSG00000114867">https://identifiers.org/ensembl/ENSG00000114867</a>	<a href="https://identifiers.org/hcigene/1981">https://identifiers.org/hcigene/1981</a>
EIF4EBP1	<a href="https://identifiers.org/ensembl/ENSG00000197840">https://identifiers.org/ensembl/ENSG00000197840</a>	<a href="https://identifiers.org/hcigene/1978">https://identifiers.org/hcigene/1978</a>
MMP2	<a href="https://identifiers.org/ensembl/ENSG00000087245">https://identifiers.org/ensembl/ENSG00000087245</a>	<a href="https://identifiers.org/hcigene/4313">https://identifiers.org/hcigene/4313</a>
MMP14	<a href="https://identifiers.org/ensembl/ENSG00000157227">https://identifiers.org/ensembl/ENSG00000157227</a>	<a href="https://identifiers.org/hcigene/4323">https://identifiers.org/hcigene/4323</a>
MTOR	<a href="https://identifiers.org/ensembl/ENSG00000198793">https://identifiers.org/ensembl/ENSG00000198793</a>	<a href="https://identifiers.org/hcigene/2475">https://identifiers.org/hcigene/2475</a>



WikiPathways  
Pathways for the People

**Figure 2: Using SPARQL to extract all genes from the Malignant Pleural Mesothelioma (MPM) molecular pathway in WikiPathways (WP5087).** Using the WikiPathways SPARQL endpoint ([sparql.wikipathways.org](http://sparql.wikipathways.org)), a SPARQL query can be written (top) to produce a table (bottom) containing all genes of the MPM molecular pathway.



**Figure 3: Using federated SPARQL to extract all proteins of the Malignant Pleural Mesothelioma (MPM) molecular pathway annotated with the GO term "DNA-repair" or one of its children.** Using the neXtProt SPARQL endpoint ([sparql.nextprot.org](http://sparql.nextprot.org)), a SPARQL query can be written (left) to produce a table (right) containing all proteins of the MPM molecular pathway with a role in DNA repair processes according to Gene Ontology (GO) annotation.

### How to contribute

The PM molecular pathway model encourages community-driven engagement and contributions, fostering continuous improvement. Researchers and clinicians can actively participate by proposing additions, curating, and sharing the pathway. This collaborative approach enables the pathway model to evolve, incorporating the latest research findings and insights from the community, ultimately enhancing our understanding of malignant pleural mesothelioma at the molecular level.

### References

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2. Kutmon M, et al. (2015) PathVisio 3: an extendable pathway analysis toolbox. doi:10.1371/journal.pcbi.1004085
3. Martens M, et al. (2022) A Community-Driven, Openly Accessible Molecular Pathway Integrating Knowledge on Malignant Pleural Mesothelioma. doi:10.3389/fonc.2022.849640
4. Zahn-Zabal M, et al. (2020) The neXtProt knowledgebase in 2020: data, tools and usability improvements. doi:10.1093/nar/gkz995