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Detecting recurrent gene mutation in interaction network context using multi-scale graph diffusion

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Summary

We introduce a multi-scale kernel diffusion framework and apply it to a large collection of murine retroviral insertional mutagenesis data. The diffusion strength plays the role of scale parameter. As a result, in addition to detecting genes with frequent mutations in their **genomic vicinity** (red nodes in the interaction graph) we can also find genes that harbor frequent mutations in their **interaction network context** (white and pink nodes).

Methods			
Interaction Graph	Multi-scale Graph Diffusion	Permutation Analysis	Significant Genes Clusters
	Scale Prameter: Diffusion Strength (B)		



White and Pink ReMIC genes are co-localized in Leukemia Pathway



ReMIC clusters are enriched for cancer related pathways



Conclusion

We identify densely connected components of known and novel cancer genes. They are strongly enriched for cancer related pathways across the diffusion scales. The mutations in the clusters exhibit a **significant pattern of mutual exclusion**. The results demonstrate the importance of defining recurrent mutations in the **interaction network context** at **multiple scales**.

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