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Citation (APA)

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

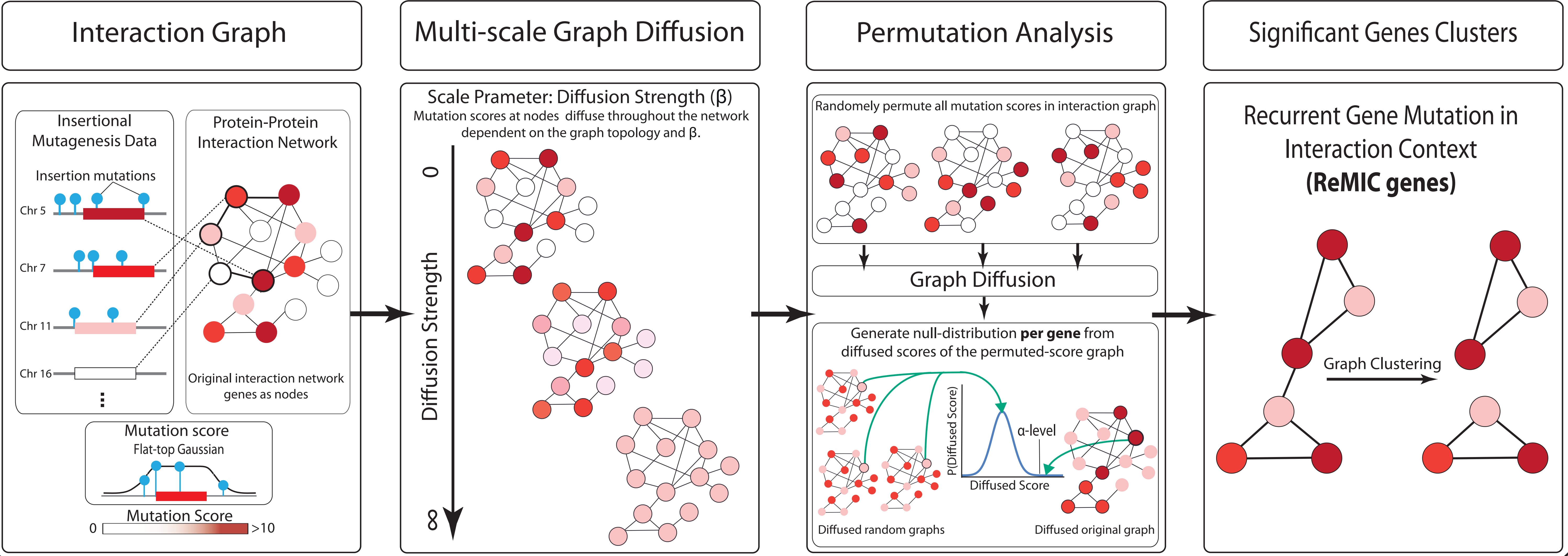
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¹Delft Bioinformatics Lab, Delft University of Technology, ²Netherlands Bioinformatics Center.

Summary

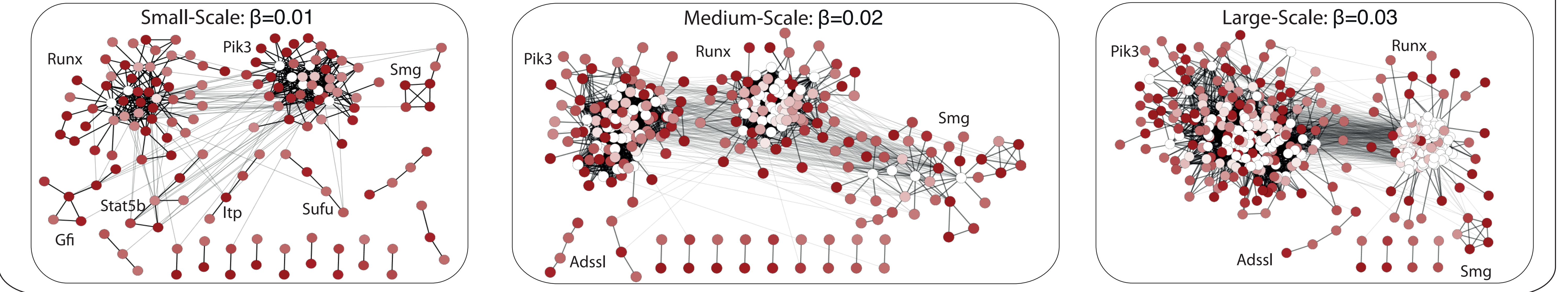
We introduce a multi-scale kernel diffusion framework and apply it to a large collection of murine retroviral insertional mutagenesis data. The diffusion strength plays the role of scale parameter. As a result, in addition to detecting genes with frequent mutations in their **genomic vicinity** (red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

Methods

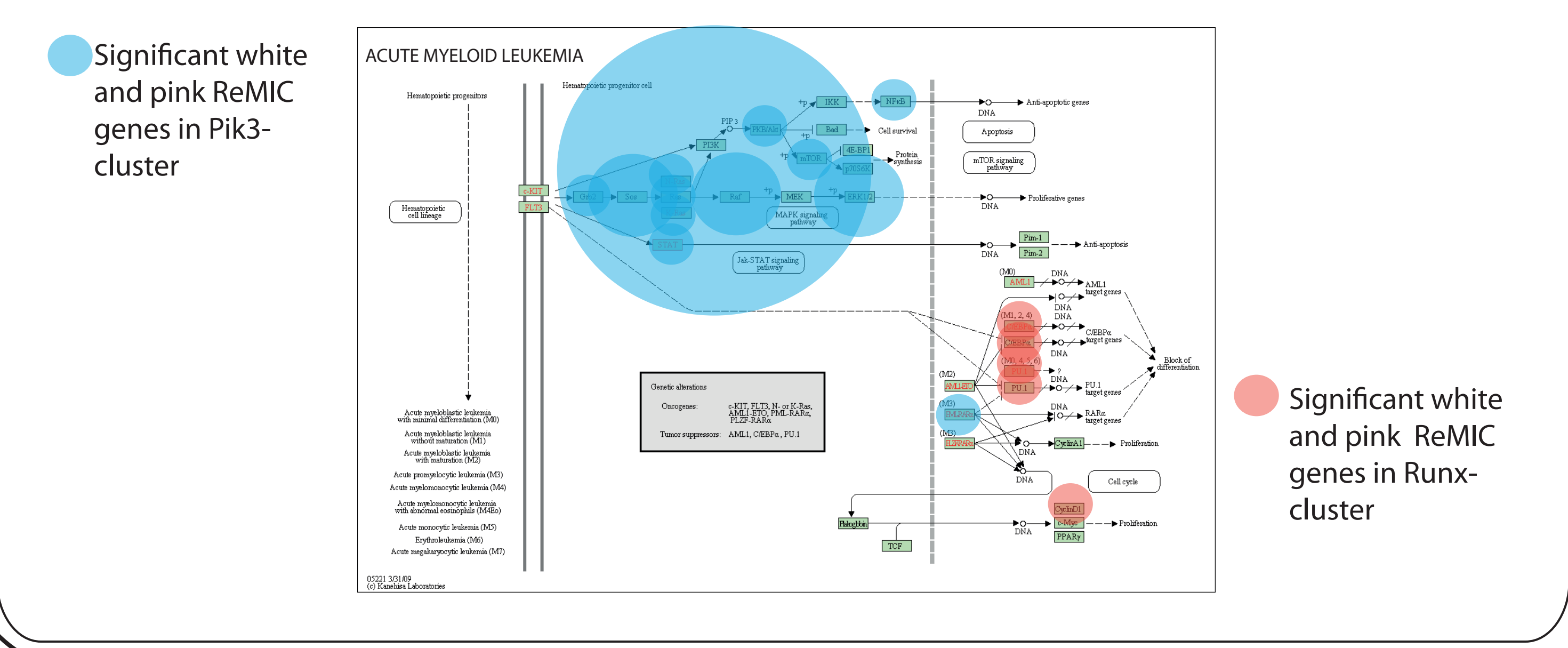


Results

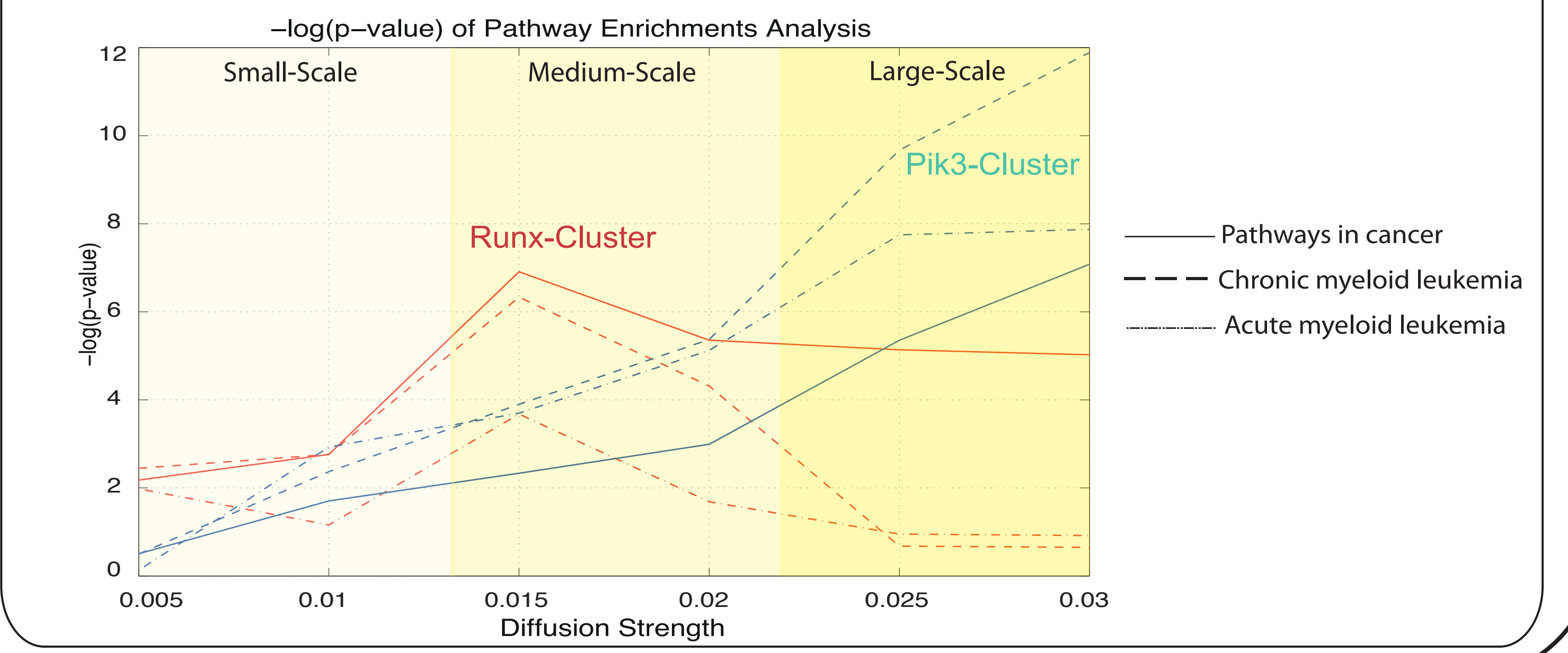
ReMIC genes clusters in 3 diffusion scale-levels



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**.

Acknowledgments: The author is supported by the **Swiss Foundation for Excellence and Talent in Biomedical Research** fellowship to attend ECCB12.