

From Mutation Analysis to Pathways and Back: Interoperability between CRAVAT/MuPIT and NDEX

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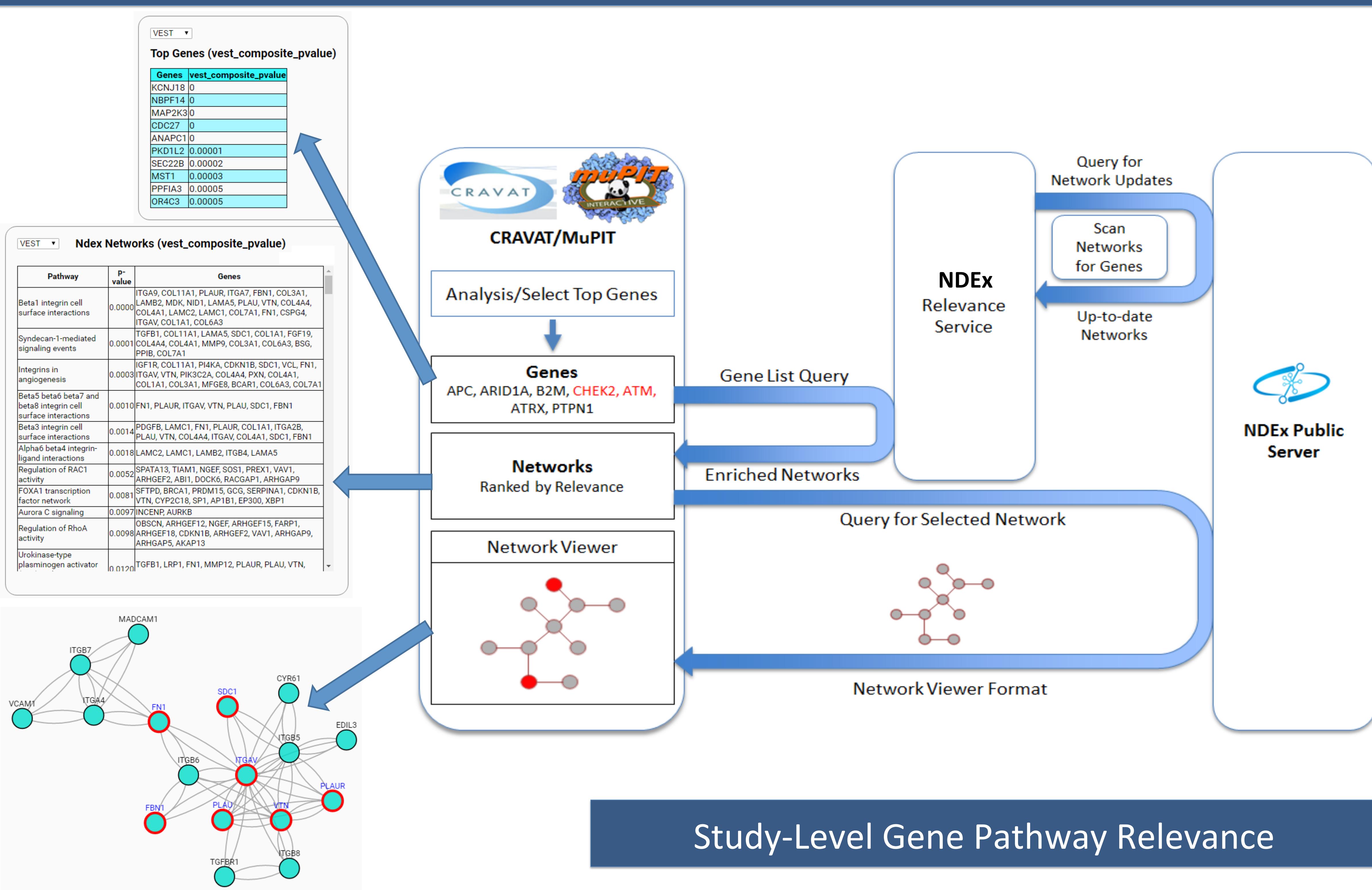
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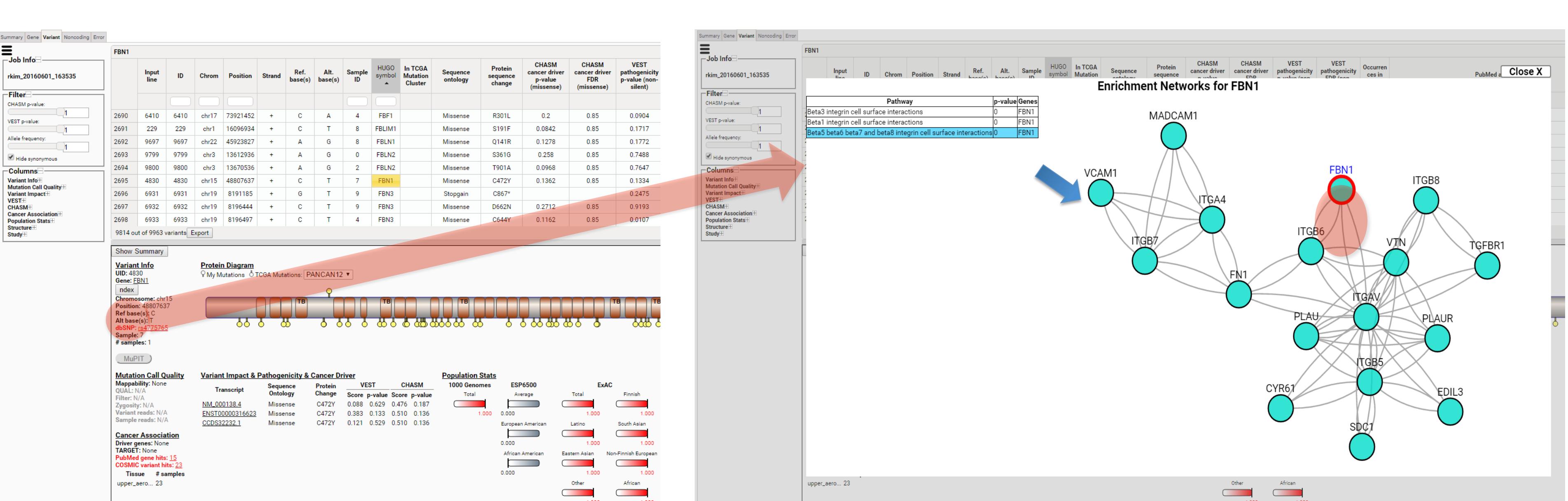
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Abstract

Communication and interoperability among bioinformatics services can create synergy which significantly increases the types of information that is easily available to users and delivers integrated analysis that accelerates biological insights. We present a successful collaboration between CRAVAT/MuPIT, which is a genomic variant annotation service, and NDEx, which is a biological network data exchange service. From mutation-call input, CRAVAT/MuPIT extracts a list of genes that are predicted to be the most pathogenic or most likely to be cancer drivers, and passes this list to the Relevance Service on the NDEx server, which was specifically developed for this collaboration. The Relevance Service returns the biological networks that are most enriched in the high scoring CRAVAT genes. Users then select biological networks of interest which are visualized in CRAVAT with data from the public NDEx server. The integration of gene networks into CRAVAT greatly increases the context we are able to give researchers investigating genetic mutations and has allowed NDEx to develop new services which will benefit a wide range of bioinformatics tools.



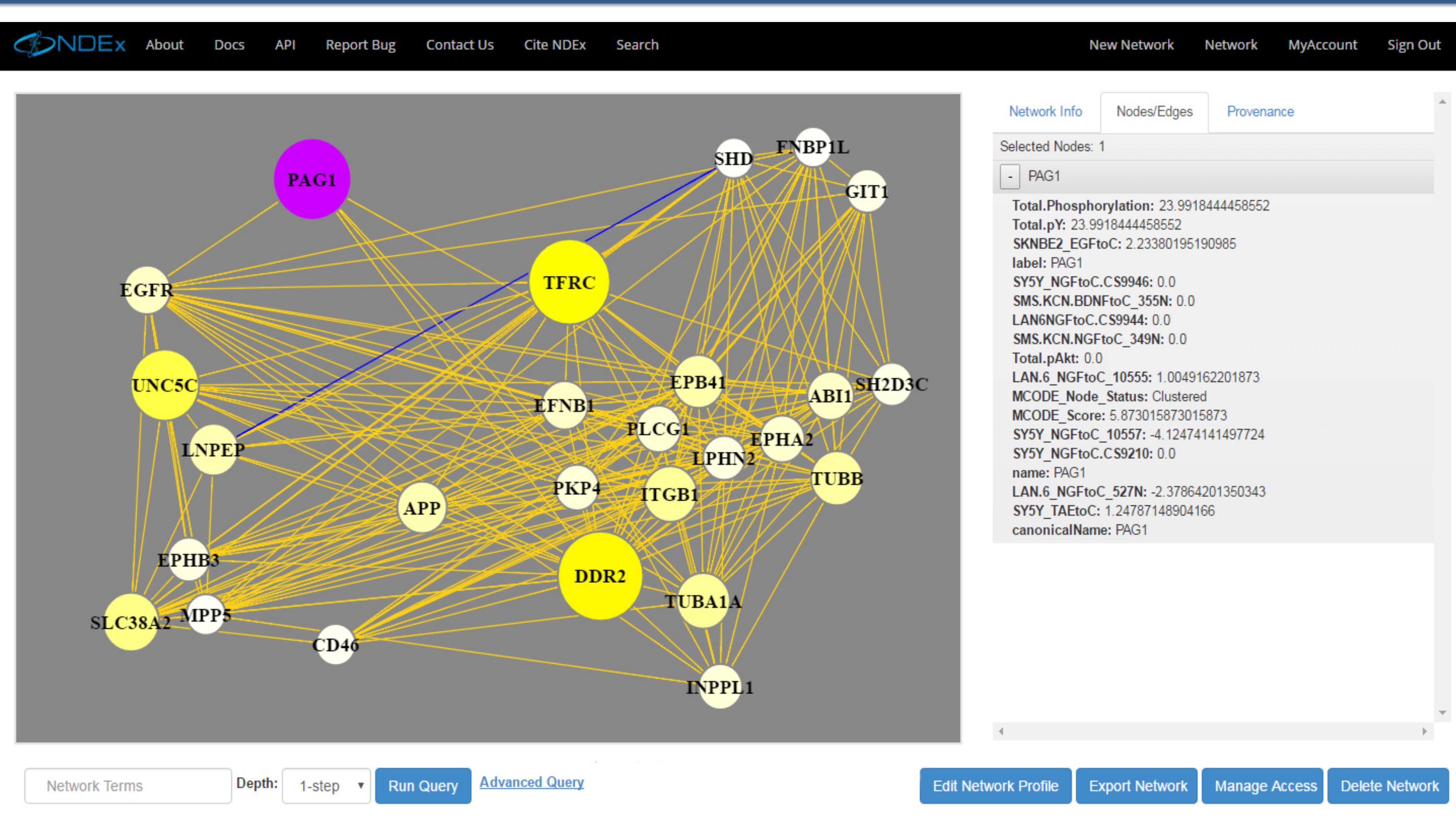
Individual Variant Relevance Lookup



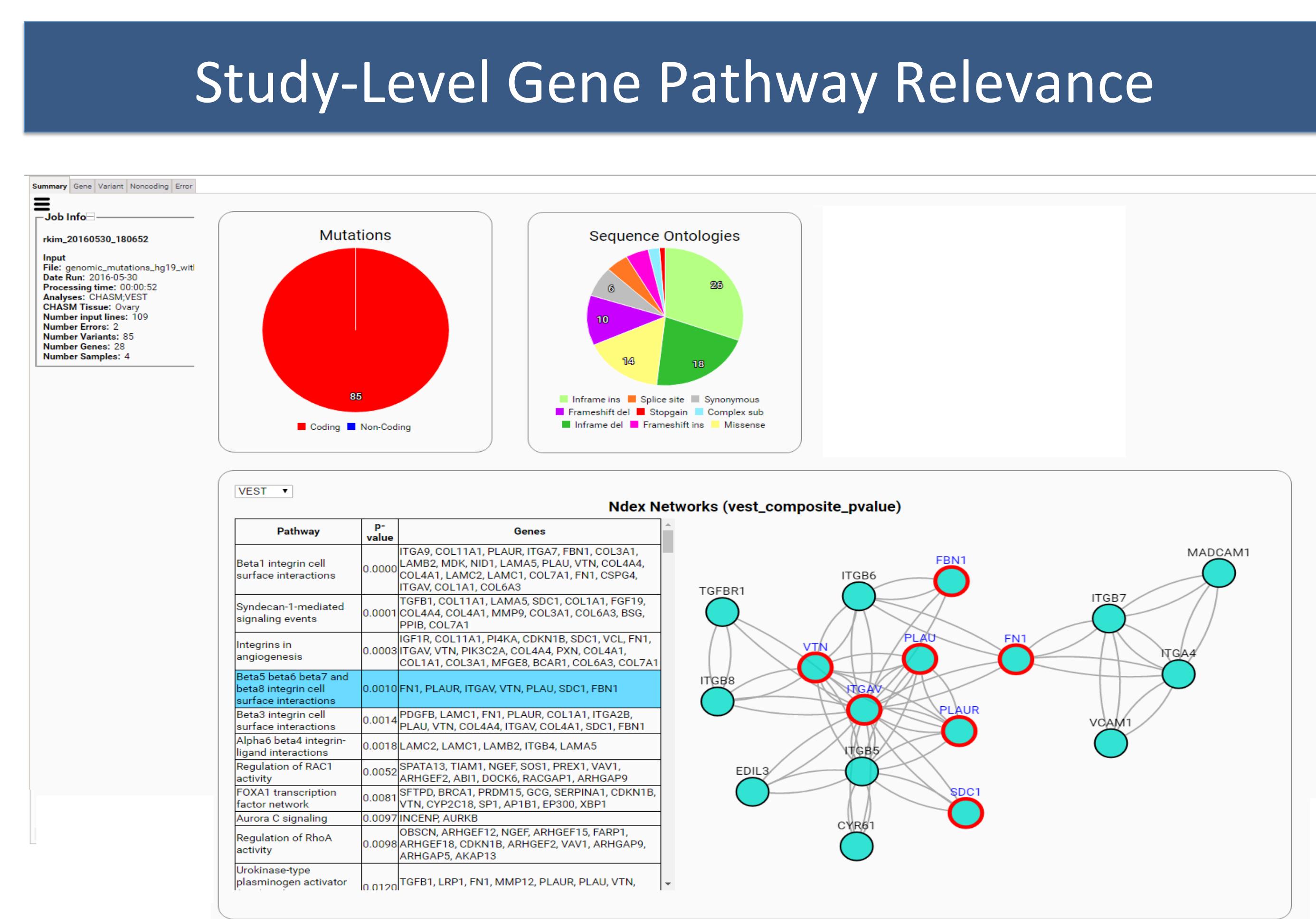
Retrieve the networks

Selected network is visualized with the
input layer highlighted

New NDEFx Network Visualization Page



Informative dynamic visualization of NDEx networks in CRAVAT/MuPIT required changes to be implemented in the new Network Visualization page of the NDEx web UI.



Genes with the highest predicted variant impact.

Selected network is visualized
(query genes highlighted).

Conclusion

The collaboration with the CRAVAT/MuPIT team has provided a valuable application case for the NDEx Project, contributing to the development of NDEx-enabled services, improved web visualization of networks and guidelines for network formats. For this collaboration, the NDEx Project built a Python-based “Relevance Service” that could index sets of pathway networks stored in NDEx and then respond rapidly to queries, returning lists of networks ranked by their relevance to the queried gene list. The relevance service is a reusable module that will be adapted for use in the main NDEx web user interface (UI). Similarly, the need to dynamically visualize CRAVAT/MuPIT analysis result data mapped to NDEx networks helped prototype changes that are now being incorporated in the new Network Visualization page for the NDEx web UI. Finally, the need to present clear, informative networks to CRAVAT/MuPIT users has resulted in an ongoing review of the simplified SIF format for “NCI-Pathway Interaction Database” networks thus contributing to the development of annotation guidelines for simple networks.

References

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 - Pratt D, Chen J, Welker D, Rivas R, Pillich R, Rynkov V, Ono K, Miello C, Hicks L, Szalma S, Stojmirovic A, Dobrin R, Braxenthaler M, Kuentzer J, Demchak B, Ideker T (2015). **NDEx: the Network Data Exchange**. Cell Systems, 1(4):302-305.