

P2.151: Comprehensive Characterization of the Fusion Landscape and Fusion Burden in Non-Small Cell Lung Cancer Using Tissue RNA-Seq

Authors: D. Enrico^{1,2,3}, R. Borea^{1,2}, F. Drago^{1,2}, L. Cozzone^{1,2}, E. Shankar^{1,2}, G. Nigita^{1,2,4,5}, C. Rolfo^{1,2}

¹The Arthur G. James Comprehensive Cancer Center, The Ohio State University, Columbus/OH/USA, ²The Ohio State University, Columbus/OH/USA, ³Alexander Fleming Cancer Institute, Buenos Aires/AR, ⁴Center for RNA Biology, The Ohio State University, Columbus, Ohio, USA, ⁵Pelotonia Institute for Immuno-Oncology, The Arthur G. James Comprehensive Cancer Center, The Ohio State University, Columbus, Ohio, USA

Correspondence: Diego.Enrico@osumc.edu; Christian.Rolfo@osumc.edu



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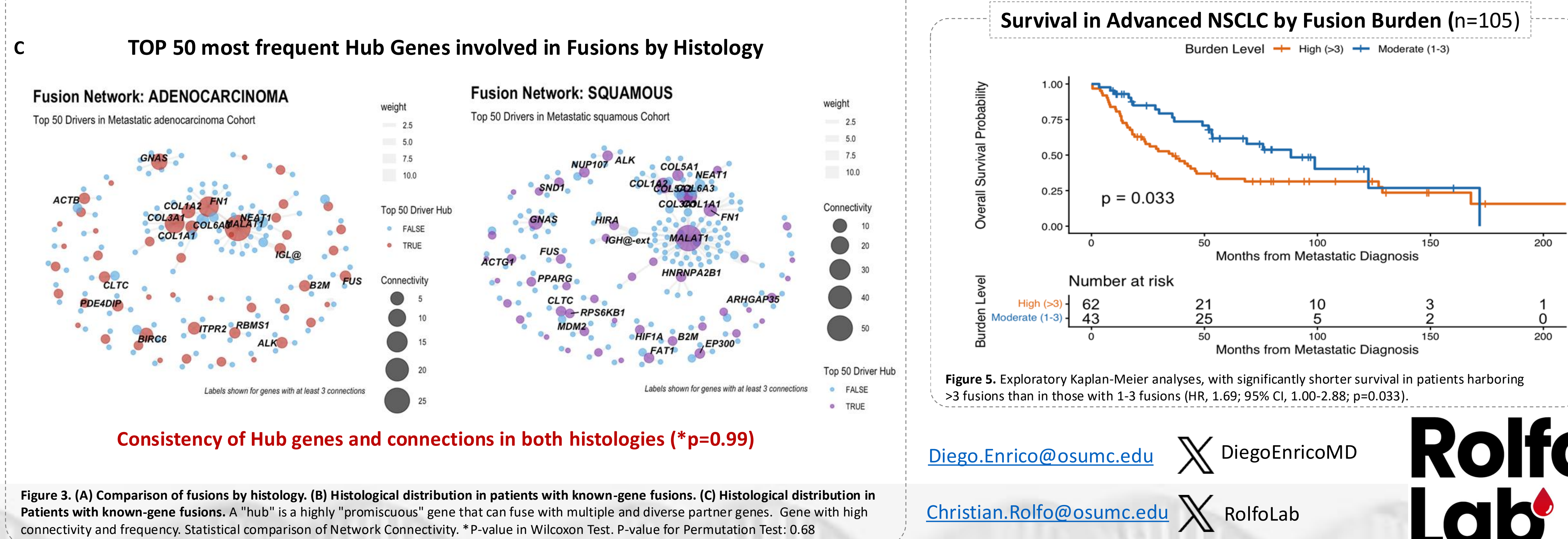
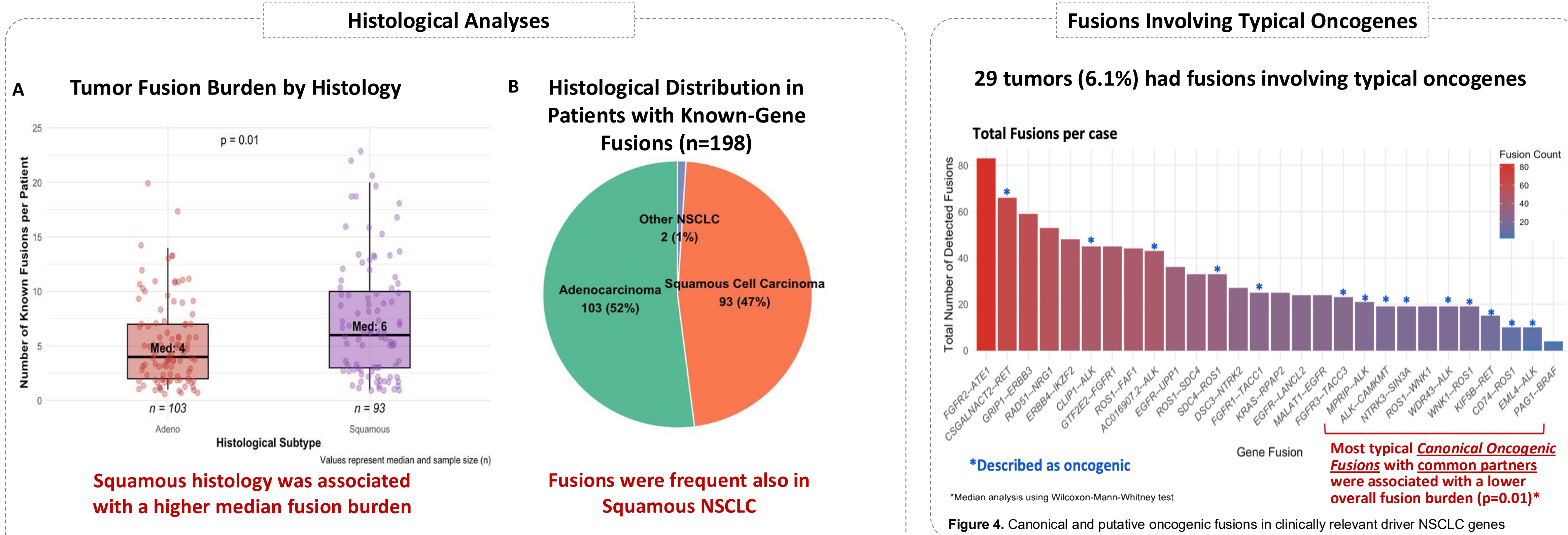
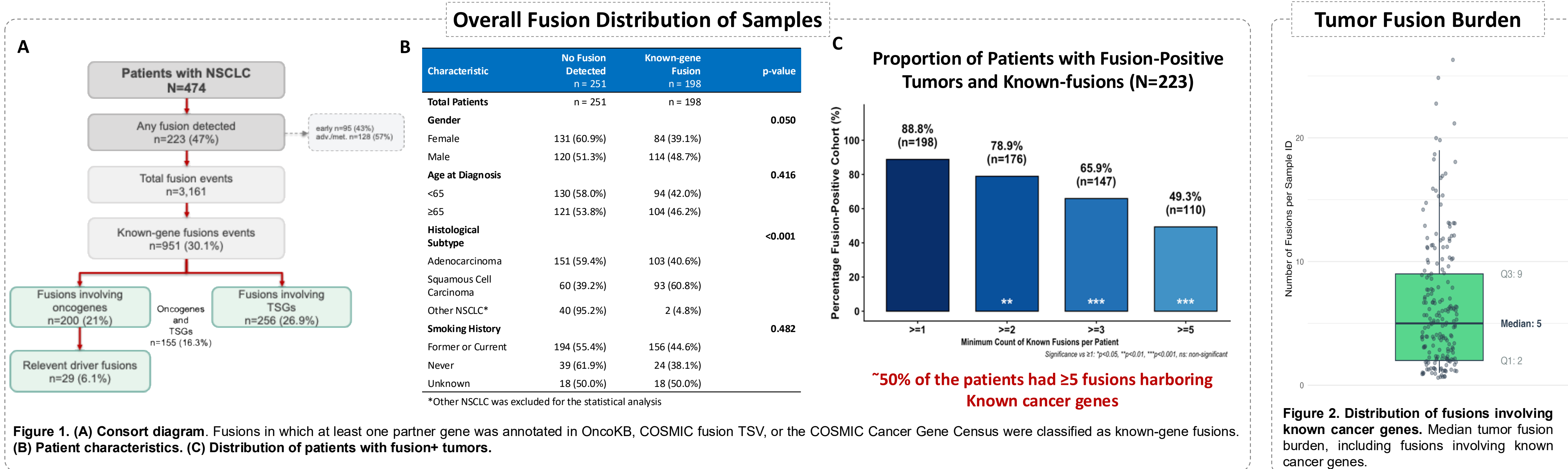
INTRODUCTION

- The identification of oncogenic driver alterations has profoundly transformed the natural history of non-small cell lung cancer (NSCLC).
- Gene fusions** have emerged as key actionable drivers with substantial evidence supporting their clinical relevance.
- However, most studies have focused on well-established fusion actionable drivers, whereas the **broader fusion landscape remains insufficiently characterized**.
- We aimed to **comprehensively analyze RNA fusion events in NSCLC** and assess their **clinicopathologic associations**.

METHODS

- We analyzed patients with NSCLC enrolled in the **Total Cancer Care Protocol at The Ohio State University** Comprehensive Cancer Center who underwent research-grade RNA sequencing of primary or metastatic tumor tissue after providing signed consent (IRB20252132).
- Gene fusions were identified using the ARRIBA and STAR-Fusion pipelines. Fusions involving cancer genes annotated in OncoKB or COSMIC were classified as "known-gene fusions".
- We evaluated tumor fusion burden (total number of unique RNA-level fusions per sample), classical oncogenic driver fusions, clinicopathologic associations, and exploratory overall survival analyses restricted to patients with advanced NSCLC.

RESULTS



DISCUSSION AND CONCLUSION

Actionable Take Away Message

- NSCLC exhibits a complex and heterogeneous fusion landscape beyond canonical targetable rearrangements. Although many RNA sequencing-detected fusions were likely biologically incidental, a subset involving known cancer genes occurred across different NSCLC histologic subtypes.

Future Direction for Research

- These findings suggest that fusion burden may have clinical relevance in NSCLC; however, systematic strategies integrating clinical context, structural and functional evidence features are needed to prioritize potentially meaningful fusions.

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Diego.Enrico@osumc.edu X DiegoEnricoMD

Christian.Rolfo@osumc.edu X RolfoLab

Rolfo
Lab