XIX CONGRESSO NAZIONALE SIES 2026

NONO modula la progressione del mieloma multiplo attraverso percorsi dipendenti ed indipendenti dalle paraspecole

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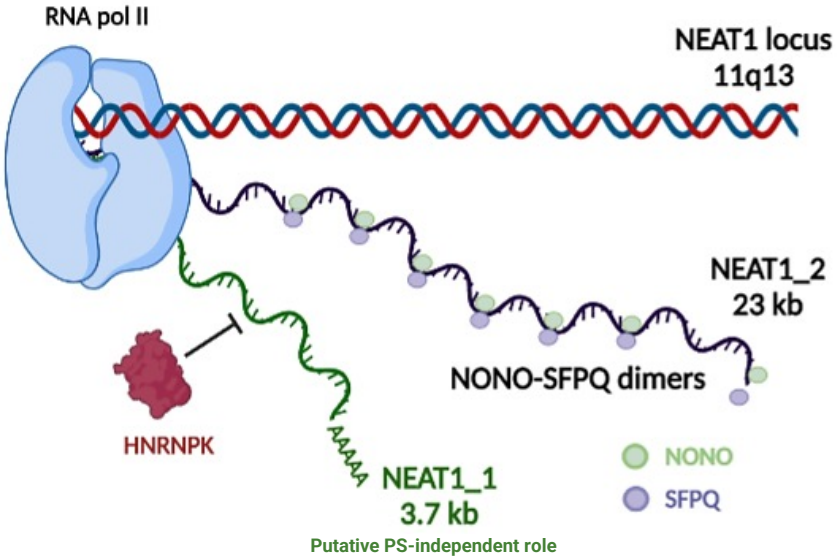
Palazzo degli Affari

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other



Putative PS-independent role

haematologica
Journal of The Ferrata Storti Foundation

Long Non-Coding RNA NEAT1 Shows High Expression Unrelated To Molecular Features And Clinical Outcome In Multiple Myeloma

Elisa Taiana, Domenica Ronchetti, Vanessa Favasuli, Katia Todoerti, Martina Manzoni, Nicola Amodio, Pierfrancesco Tassone, Luca Agnelli, Antonino Neri

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Activation of long non-coding RNA NEAT1 leads to survival advantage of multiple myeloma cells by supporting a positive regulatory loop with DNA repair proteins

Elisa Taiana,[1,2] Cecilia Bandini,[3,4] Vanessa Katia Favasuli,[1,2] Domenica Ronchetti,[1,2] Ilaria Silvestris,[1,2] Noemi Puccio,[1,2] Katia Todoerti,[1] Silvia Erratico,[5,6] Domenica Giannandrea,[7] Niccolò Bolli,[1,2] Nicola Amodio,[8] Alessia Ciarrocchi,[9] Raffaella Chiaramonte,[7] Yvan Torrente,[6] Roberto Piva[3,4] and Antonino Neri[1,2*]

Leukemia

Long non-coding RNA NEAT1 targeting impairs the DNA repair machinery and triggers anti-tumor activity in multiple myeloma.

Taiana E[1,2], Favasuli V[1,2], Ronchetti D[1,2], Todoerti K[1,2], Pelizzoni F[2], Manzoni M[1], Barbieri M[2], Fabris S[2], Silvestris I[1], Gallo Cantafio ME[3], Platonova N[4], Zuccalà V[5], Maltese L[5], Soncini D[6], Ruberti S[6], Cea M[6], Chiaramonte R[4], Amodio N[3], Tassone P[3,7], Agnelli L[1], Neri A[8,9].

NONO/p54^{nrb} (Nuclear RNA-binding protein, 54 kDa)

- overexpressed in MM PCs as compared to healthy donors-derived PCs
- associated with poor OS and PFS
- correlated with high-risk molecular subtypes
- linked to activation of cell cycle pathways
- associated with upregulated DNA repair mechanisms
- involved in deregulated RNA processing and splicing

- a potential prognostic biomarker
- a potential therapeutic target

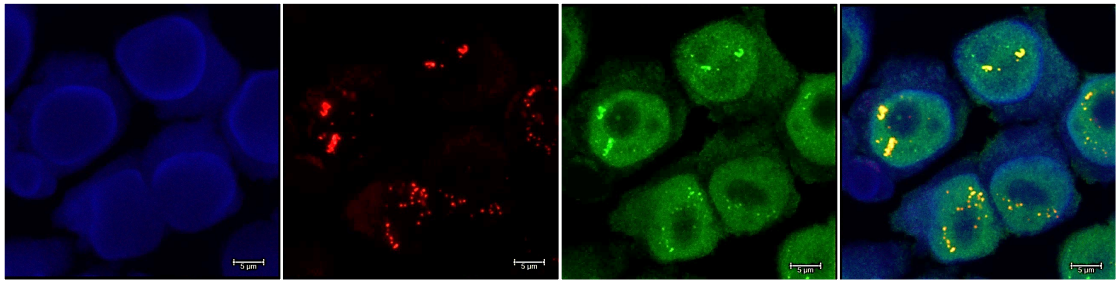
Discover Oncology

Discover

Brief Communication

Expression levels of NONO, a nuclear protein primarily involved in paraspeckles function, are associated with several deregulated molecular pathways and poor clinical outcome in multiple myeloma

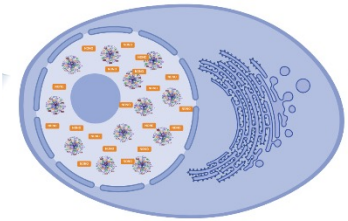
Domenica Ronchetti[1,2] · Vanessa Katia Favasuli[1,2] · Ilaria Silvestris[1,2] · Katia Todoerti[1,5] · Federica Torricelli[3] · Niccolò Bolli[1,2] · Alessia Ciarrocchi[3] · Elisa Taiana[1] · Antonino Neri[4]



Aim of the study

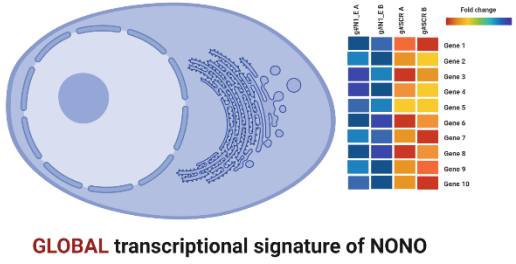
To define how NONO shapes the transcriptomic landscape of MM plasma cells, both through its PS-associated and independent mechanisms

Experimental design

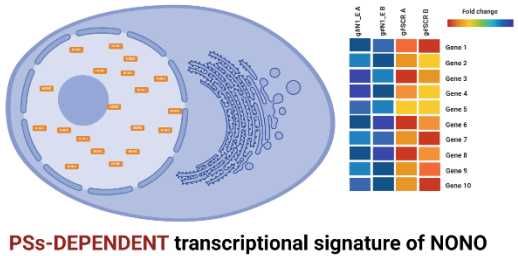


NONO within PSs

NONO out side PSs NONO



GLOBAL transcriptional signature of NONO

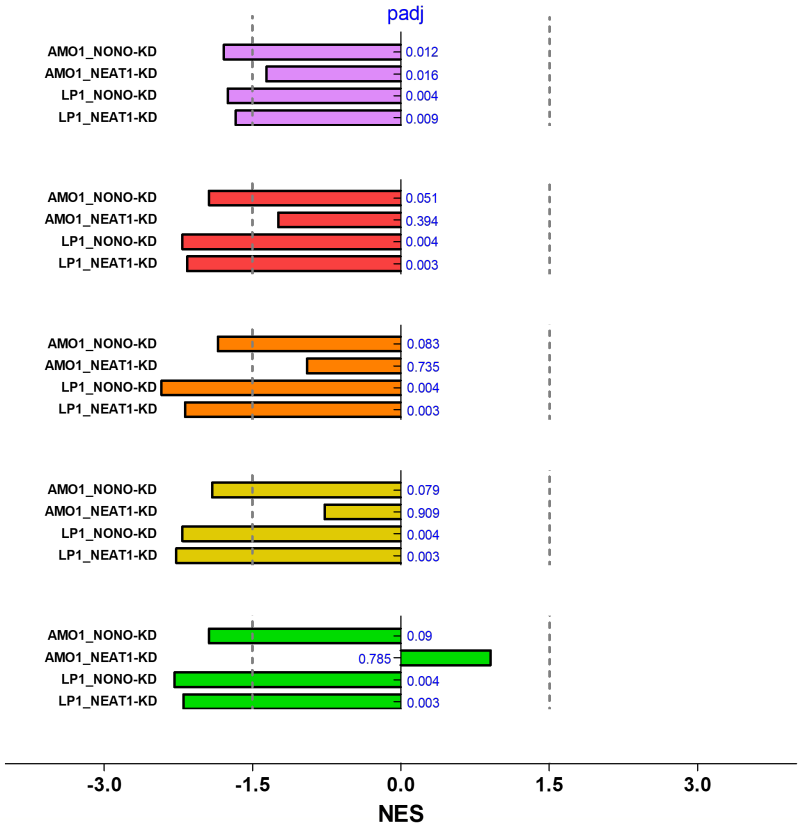


PSs-DEPENDENT transcriptional signature of NONO

Shared pathways between NONO-KD and NEAT1-KD samples will shed light on NONO's functions related to PS

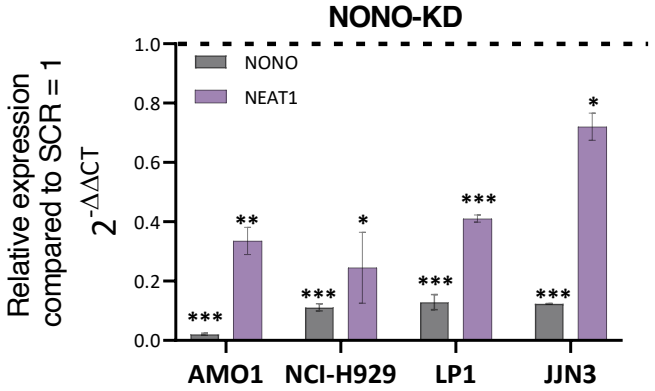
NONO-KD specific pathways will be suggestive of its PS-independent role.

NONO's involvement in PS-associated pathways



REACTOME_SIGNALING_BY_NOTCH
REACTOME_RUNX1_REGULATES_GENES_INVOLVED_IN_MEGAKARYOCYTE_DIFFERENTIATION_AND_PLATELET_FUNCTION
REACTOME_HDACS_DEACETYLATE_HISTONES
REACTOME_FORMATION_OF_THE_BETA_CATENIN_TCF_TRANSACTIVATING_COMPLEX
REACTOME_DNA_METHYLATION

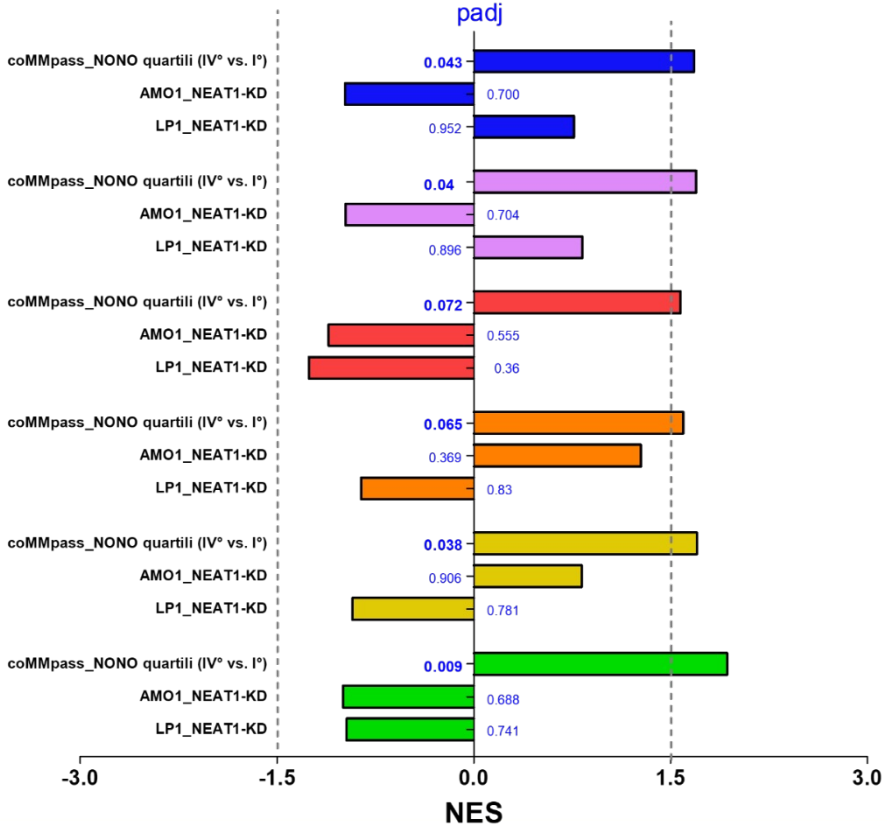
NONO's involvement in PS-unrelated pathways



The transcriptomic alterations observed upon NONO silencing could be, at least partially, driven by NEAT1 downregulation, thereby reflecting PS-dependent effects

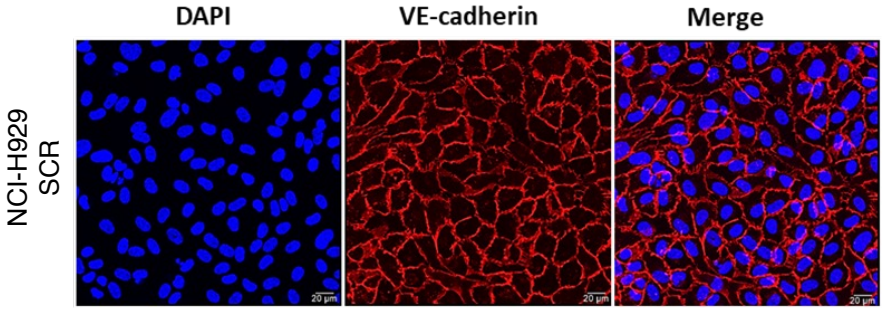
Highest vs. lowest quartiles of NONO expression (CoMMpass dataset)
→ identification of distinct pathways not shared with NEAT1-KD HMCLs

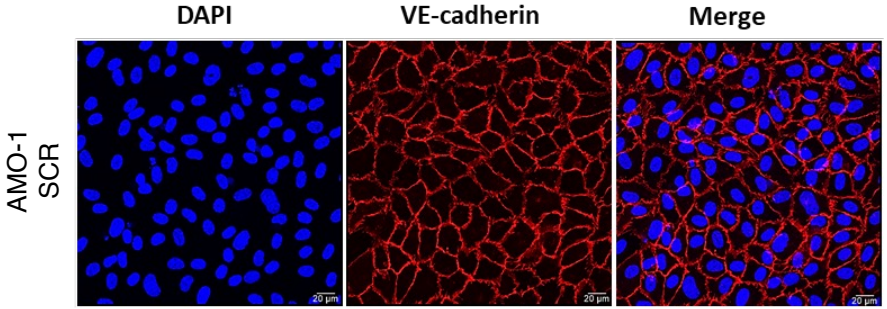
NONO's involvement in PS-unrelated pathways



- REACTOME_TRANS_GOLGI_NETWORK_VESICLE_BUDDING
- REACTOME_GOLGI_ASSOCIATED_VESICLE_BIOGENESIS
- REACTOME_MITOCHONDRIAL_BIOGENESIS
- REACTOME_CELL_CELL_JUNCTION_ORGANIZATION
- REACTOME_CELL_CELL_COMMUNICATION
- REACTOME_PROCESSING_OF_INTRONLESS_PRE_MRNAS

HUVEC cells cultured with conditioned medium from





Take-Home Messages

- The comparison of NONO-related and NEAT1-related signatures reveals substantial overlap linked to PSs biology, while also identifying PS-independent roles of NONO.
- The observed dysregulation of cell-cell adhesion pathways following NONO-KD highlights a previously underappreciated role for NONO in modulating the tumour microenvironment.

Conclusions

This study highlights the potential of NONO as a therapeutic target in MM by elucidating its role in transcriptional regulation, particularly within pathways essential to disease progression.

Acknowledgments

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