Novel piRNA Landscape of Extracellular Vesicles in Osteoarthritis Pathology

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PURPOSE:

Extracellular vesicles(EVs) are released by cells into body fluid under physiological and pathological conditions[1,2]. Emerging research focuses on the EVs cargo contents, including small non-coding RNA(sncRNAs), and their potential applications for diagnostic and therapeutic purposes. We hypothesized that the expression levels of piwi-interacting RNA (piRNA), a novel subtype of sncRNA, were dysregulated in osteoarthritis(OA) individuals. Our objective was to identify EV-piRNAs in OA and non-OA plasma(PB) and synovial fluid(SF).

MATERIALS & METHODS:

OA and non-OA PB and SF procured from consented arthroplasty and arthroscopy subjects respectively(UMMC ethics approval number: 20211029-10716), were subjected to EV-total RNA extraction, using an exoRNeasy kit. Fifty nanograms of total RNA were used for Illumina NovaSeq small RNA sequencing. piRNA identification was then conducted via the exceRpt pipeline. Only piRNA with RPM(read per million) ≥10 in at least two individuals were included for piRNA target prediction, DAVID pathways analysis and qRT-PCR validation analysis.

RESULTS:

A total of 48 piRNAs were commonly expressed in both the PB and SF(Figure 1); 3 piRNAs and 31 piRNAs were identified as only expressed in PB and SF, respectively. Based on piRNA target prediction analysis, commonly-expressed piRNAs in OA PB and SF(i.e. piRNAs targeting *BCL9*, *BANK1*, *MTRNR2* and *TERF2*) are potentially involved in chondrocyte terminal differentiation, apoptosis and DNA damage response.

DISCUSSIONS:

Based on the findings from this study, the hypothetical pathways of the identified piRNA candidates are PI3K/AKT, WNT/β-catenin and intrinsic apoptosis signalling pathways(Figure 2), which their dysregulations result in cartilage degeneration and OA development/progression. These piRNAs are potential biomarkers for OA diagnosis, as they can be detected non-invasively in PB, allowing OA to be diagnosed via blood samples without the need for arthrocentesis(i.e., synovial fluid aspiration).

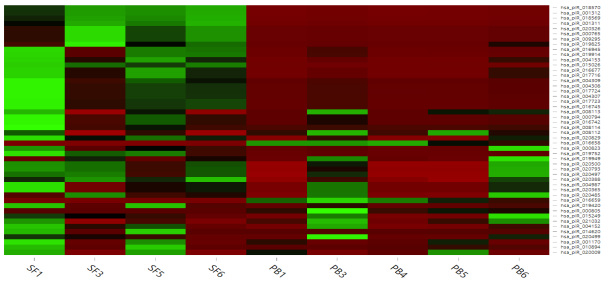

Figure 1: Heatmap of EV-piRNA commonly expressed in PB and SF.

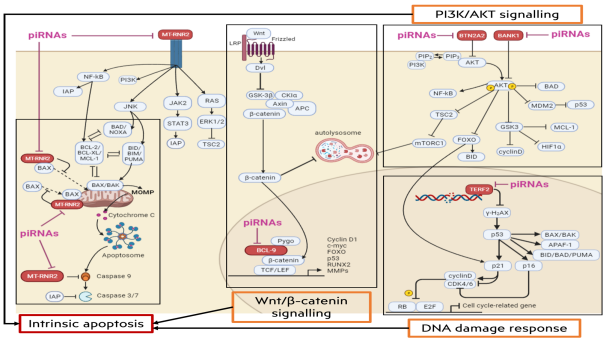

Figure 2: Hypothetical pathways of piRNA candidates.

CONCLUSION:

EV-piRNAs were identified in PB and SF. Further analysis with functional assay is required to validate their roles in OA pathology.

REFERENCES:

1.Yates, Abi G et al. 2022. *Journal of Extracellular Vesicles* 11(1): e12151.
2.Goh, TX et al. 2022. *Tissue Engineering Part C* 28(10):511-528.