FGFR1/FGFR1 isoforms accelerate prostate cancer progression to metastasis

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Background. Bone metastases typically develop in patients with advanced prostate cancer (PCa). We have previously reported that the fibroblast growth factor (FGF) axis is implicated in the pathogenesis of PCa bone growth, and that FGFR blockade has clinical activity in advanced PCa and bone metastases (PMID:25186177).

Methods and Results. In an RNA sequencing study of 183 human PCas we found that different samples express different FGFR1 transcripts. We then mined the TCGA PCa database to determine the expression profile associated with two well characterized FGFR1 splice variants, alpha and beta, which represent the most abundant protein coding transcripts found in PCa. We discovered that each isoform is associated with expression of different genes. Also, in gene set enrichment analysis, we found that FGFR1 beta (but not alpha) is associated with many pathways. In particular, FGFR1 beta is significantly associated with MAPK signaling cascade, signaling by FGFR in disease, and pathways in cancer, among others. *In vitro* studies of FGF signaling activation in PCa cells expressing FGFR1 isoforms alpha, beta or empty vector (EV), confirmed these results. Therefore, these results suggest that FGFR1 alpha and beta induce different genes. Importantly, when compared to PCa cells expressing EV, PCa cells expressing FGFR1 isoforms produce significantly more metastasis and reduced survival of mice injected intracardially with the cells. Furthermore, we found a significant increase of bone metastases in the group of mice injected with PC3 FGFR1 alpha and beta compared to PC3 EV. These results suggest that FGFR1 accelerates the metastatic phenotype of PCa cells.

Conclusions. Our studies suggest that FGFR1 alpha and beta activate different genes and pathways in PCa cells thus conferring different phenotypes. We further propose that FGFR1 expression in PCa cells favors its metastatic dissemination to bone and this may be mediated at least partially by activating a PCa cells-bone cells interaction.

Conflict of Interest: NA.

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