The role of FXR in the osteomimicry of PC-3 prostate cancer cells

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Introduction

The majority of death in cancer is due to the presence of metastases and in prostate cancer, bone is the most common site for metastasis with 80% of metastases cases. The farnesoid X receptor (FXR) is activated by bile acids and is present in prostate carcinoma where its function is still little known. In the present study, we aim to evaluate the role of the farnesoid X receptor (FXR), a metabolic receptor activated by bile acids, in the osteomimicry of prostate cancer cell line PC-3.

Materials and methods

- **Cell proliferation – Crystal violet staining (CV)**
  - Seeding (4000 cells/well) 24h Treatment 72h Fixation Crystal Violet (CV)

- **Protein expression – Immunofluorescence (IF)**
  - Seeding (10,000 cells/well) 24h Treatment 24 or 48h Fixation Immunofluorescence (IF)

Results

Figure 1: Effect of CDCA on cell proliferation. The cell proliferation remained relatively stable between the control and cells exposed to CDCA and decreased after 40 µM of CDCA (T-Test, *: p<0.05, **: p<0.001).

Figure 2: Effect of z-guggulsterone alone or in combination with CDCA on cell proliferation. Z-guggulsterone is an antagonist of FXR. This treatment decreased the cell proliferation. The two curves almost overlapped. (T-test, *: p<0.05, **: p<0.001).

Figure 3: Effect of lithocholic acid in combination with CDCA on cell proliferation. Lithocholic acid is a bile acid and a competitive inhibitor of FXR. The two curves remained relatively stable and decreased after 40 µM of LCA (LCA and LCA+CDCA). No difference was observed between the two curves. (T-test, *: p<0.05, **: p<0.001).

Figure 4: FXR expression in PC-3 prostate cell line. FXR was expressed in the nucleus and in the cytoplasm of cells. CDCA treatment (CDCA) increased FXR expression versus control cells (C).

Figure 5: RUNX2 expression after different treatments for 24h. RUNX2 is expressed and located in the nucleus. CDCA: > RUNX2 expression compared to the control (C) CDCA+G, CDCA+LCA: \ RUNX2 expression compared to CDCA. G, LCA: no difference versus the control

Figure 6: Osteoponitin (OPN) expression after different treatments for 48h. OPN is expressed and located in the cytoplasm. CDCA: > OPN expression compared to the control (C) CDCA+G, CDCA+LCA: \ OPN expression compared to CDCA. G, LCA: no difference versus the control

Conclusion

Experimental data highly support a relationship between FXR and RUNX2 expression in PC-3 cells. FXR promotes the propensity of tumor cells to develop osteomimicry, involving a possible mechanism stimulating RUNX2 and a subsequent induction of bone-related protein synthesis.

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