**Role of Host GPR120 in Mediating Dietary Omega-3 Fatty Acid Inhibition of Prostate Cancer**

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**Background:** GPR120, a G protein-coupled receptor for long chain polyunsaturated fatty acids (FAs), mediates the anti-inflammatory effects of omega-3 (ω-3) FAs. We investigated whether host or tumor GPR120 plays a role in the anti-prostate cancer effects of ω-3 FAs.
**Methods:** MycCap prostate cancer allografts were grown in immunocompetent wild type (WT) and GPR120 knockout (KO) mice fed ω-3 (fish oil) or ω-6 (corn oil) diets. Immune cell infiltration was quantified by flow cytometry, and gene expression of immune cell markers in isolated tumor associated macrophages (TAMs) by RTqPCR. Archived tissue from a fish oil intervention trial was used to correlate gene expression of GPR120 with cell cycle progression (CCP) genes and Ki67 index (n=11-15 per group).
**Results:** In WT mice (n=7 per group), dietary ω-3 FAs decreased MycCap allograft tumor growth (6: 491 ±437 $mm^3$, ω-3: 127±77 $mm^3$, p=0.04), whereas in global GPR120KO mice (n=7 per group) ω-3 FAs had no anticancer effects. When knocking out GPR120 in MycCap cells GPR120KO-MycCaP dietary ω-3 FAs inhibited GPR120KO-MycCaP allografts grown in WT mice (n=8 per group) (ω-6: 776±767 $mm^3$, ω-3: 36±34 $mm^3$, p=0.02). Omega-3 FA treatment decreased the number of M2-like TAMs in tumor tissue and gene expression of M2 markers in isolated TAMs compared to ω-6 controls in WT (n=7 per group), but not in GPR120KO mice (n=7 per group). In human tissue, higher expression of stromal GPR120 correlated with greater reduction in expression of CCP genes in men with prostate cancer on a high ω-3 diet (r=-0.57; p=0.042).
**Conclusion:** Host GPR120 plays a central role in the anti-prostate cancer effects of dietary ω-3 FAs. Future studies are required to determine if the anticancer effects of ω-3 FAs are mediated through inhibition of M2-like macrophages, and if host GPR120 status predicts anticancer effects of dietary ω-3 FAs in men with prostate cancer.

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