

**Supplementary Table 5.** Literature search revealing the important pathways that are involved in aggressive prostate cancer.

| <b>LITERATURE</b>   | <b>PMID</b> | <b>Pathway</b>  |
|---|-------------|---|
| Tie-2 regulates the stemness and metastatic properties of prostate cancer cells   | 25978029    | Tie-2 protein (suppresses cancer stem cells)  |
| Diet-induced hypercholesterolemia promotes androgen-independent prostate cancer metastasis via IQGAP1 and caveolin-1.   | 25924234    | Hypercholesterolemia → orthotopic xenograft PC-3 cell metastasis = increased caveolin-1 and IQGAP1 expression   |
| Expression of spermidine/spermine N <sup>1</sup> -acetyl transferase (SSAT) in human prostate tissues is related to prostate cancer progression and metastasis. | 25893668    | Spermidine/spermine N <sup>1</sup> -acetyl transferase activation → polyamine oxidation pathway → copious reactive oxygen species in polyamine-rich PCa cells |
| SULF2 overexpression positively regulates tumorigenicity of human prostate cancer cells.  | 25887999    | SULF2 overexpression  |
| Role of Runx2 phosphorylation in prostate cancer and association with metastatic disease.   | 25867060    | Runx2 phosphorylation   |
| MYC Drives Pten/Trp53-Deficient Proliferation and Metastasis due to IL6 Secretion and AKT Suppression via PHLPP2.   | 25829425    | MYC → activates AKT phosphatase PHLPP2 in primary cells and prostate cancer metastasis  |
| Intracellular EP2 prostanoid receptor promotes cancer-related phenotypes in PC3 cells.  | 25828575    | PGE <sub>2</sub> -EP2 signalling pathway in PC3 cells   |
| YB-1 and MTA1 protein levels and not DNA or mRNA alterations predict for prostate cancer recurrence.  | 25797255    | YB-1 and MTA1 protein levels → predictors of PC relapse   |
| Over-expression of lipocalin 2 promotes cell migration and invasion through activating ERK signaling to increase SLUG expression in prostate cancer.            | 25728945    | Lipocalin 2 overexpression → ERK signalling → increased SLUG expression   |
| Downregulation of microRNA-23a suppresses prostate cancer metastasis by targeting the PAK6-LIMK1 signaling pathway.   | 25714010    | PAK6-LIMK1 signalling pathway (suppression by microRNA-23a down-regulation)   |
| miR-188-5p inhibits tumour growth and metastasis in prostate cancer by repressing LAPTM4B expression.   | 25714029    | LAPTM4B overexpression and PI3K/AKT signalling pathway  |

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| Targeting ASCT2-mediated glutamine uptake blocks prostate cancer growth and tumour development.   | 25693838 | ASCT2-mediated glutamine uptake   |
| Growth and migration of LNCaP prostate cancer cells are promoted by triclosan and benzophenone-1 via an androgen receptor signaling pathway.        | 25682003 | Androgen receptor signalling pathway: triclosan and benzophenone-1  |
| Coactivator SRC-2-dependent metabolic reprogramming mediates prostate cancer survival and metastasis.   | 25664849 | Coactivator SRC-2-dependent metabolic reprogramming   |
| CD147 modulates autophagy through the PI3K/Akt/mTOR pathway in human prostate cancer PC-3 cells.  | 25663928 | CD147 and autophagy inhibition via the PI3K/Akt/mTOR pathway  |
| The highly expressed secreted phosphoprotein 1 gene in prostate cancer metastasis: a microarray-based bioinformatic analysis.                       | 25577832 | Expression of secreted phosphoprotein 1 gene (SPP1) and PC metastasis                                     |
| Oncogenic role of the Ec peptide of the IGF-1Ec isoform in prostate.  | 25569803 | PEc overexpression  |
| PRK1/PKN1 controls migration and metastasis of androgen-independent prostate cancer cells.  |          | PRK1/PKN1 and androgen-independent prostate cancer cell metastasis  |
| Resveratrol regulates PTEN/Akt pathway through inhibition of MTA1/HDAC unit of the NuRD complex in prostate cancer.                                 | 25447541 | MTA1/HDAC → negative regulator of PTEN → facilitates survival pathways and progression of prostate cancer |
| Combination of quercetin and hyperoside inhibits prostate cancer cell growth and metastasis via regulation of microRNA-21.                          | 25354548 | inhibition of the miR-21 signaling pathway  |
| Interferon inducible antiviral MxA is inversely associated with prostate cancer and regulates cell cycle, invasion and Docetaxel induced apoptosis. | 25327819 | Loss of MxA expression → increased metastasis   |

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| The role of the RhoA/Rho kinase pathway in angiogenesis and its potential value in prostate cancer (Review).   | 25289078 | RhoA/Rho kinase (ROCK) pathway + angiogenesis in progressive PCa  |
| PI3K/Akt/mTOR pathway inhibitors enhance radiosensitivity in radioresistant prostate cancer cells through inducing apoptosis, reducing autophagy, suppressing NHEJ and HR repair pathways. | 25275598 | PI3K/Akt/mTOR pathway   |
| Tpl2 induces castration resistant prostate cancer progression and metastasis.  | 25274482 | tumor progression locus 2 (Tpl2) kinase and metastatic castration resistant prostate cancer (CRPC)  |
| TRPV6 calcium channel translocates to the plasma membrane via Orai1-mediated mechanism and controls cancer cell survival.  | 25172921 | TRPV6 calcium channel de novo expression by the PCa cell to increase its survival   |
| CXCR4 inhibition enhances radiosensitivity, while inducing cancer cell mobilization in a prostate cancer mouse model.  | 25154297 | CXCR4/CXCL12 pathway  |
| Regulation of Androgen Receptor by E3 Ubiquitin Ligases: for More or Less.   | 25152898 | ubiquitination machinery and PCa  |
| Quercetin reverses EGF-induced epithelial to mesenchymal transition and invasiveness in prostate cancer (PC-3) cell line via EGFR/PI3K/Akt pathway.  | 25150162 | Epidermal growth factor-induced epithelial-mesenchymal transition (EMT)   |
| Hsp27 regulates EGF/ $\beta$ -catenin mediated epithelial to mesenchymal transition in prostate cancer.  | 25130271 | Hsp27 in EGF-mediated EMT via modulation of the $\beta$ -catenin/Slug signaling pathway   |
| Snail regulated by PKC/GSK-3 $\beta$ pathway is crucial for EGF-induced epithelial-mesenchymal transition (EMT) of cancer cells.   | 25124796 | Snail and epidermal growth factor (EGF)/epidermal growth factor receptor (EGFR) signaling $\rightarrow$ epithelial-mesenchymal transition (EMT) |
| Penta-O-galloyl- $\beta$ -D-glucose suppresses EGF-induced eIF3i expression through inhibition of the PI3K/AKT/mTOR pathway in prostate cancer cells.                                      | 25123845 | EGF-induced eIF3i expression in the PI3K/AKT/mTOR pathway   |