S100A8 and S100A9 Target Akt, mTOR and NF-κB Signalling in Pancreatic Cancer Cells

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Context S100A8/S100A9 inflammatory proteins are suggested to be involved in pancreatic cancer (PaCa) progression. S100A8/A9 expression in the neoplastic pancreas correlate with SMAD4 mutational status suggesting possible interactions with TGF-β1.

Objective To ascertain whether S100A8/S100A9 differently affect Akt, mTOR and NF-κB signalling in PaCa cells with different aggressiveness and whether these molecules interact with TGF-β1.

Methods Western blotting analyses were used to assess the effects of S100A8, S100A9 and S100A8/A9 on Akt (Ser473, Thr308), mTOR (Ser2448) and NF-κB (p-IκB-α) in BxPC3, Capan1 and MiaPaCa2 PaCa cell lines. S100A8, S100A9, S100A8/A9 were incubated with equimolar concentrations of calcium and TGF-β1 for 24 h at 37°C. Following MALDI-TOF-MS analyses were performed. Results In BxPC3 Akt Thr308 was phosphorylated by S100A8/A9, while in Capan1 and MiaPaCa2 PaCa cells lines. S100A8, S100A9, S100A8/A9 were incubated with equimolar concentrations of calcium and TGF-β1 for 24 h at 37°C. Following MALDI-TOF-MS analyses were performed. Results In BxPC3 Akt Thr308 was phosphorylated by S100A8/A9, while in Capan1 and MiaPaCa2 PaCa cells lines. S100A8, S100A9, S100A8/A9 were incubated with equimolar concentrations of calcium and TGF-β1 for 24 h at 37°C. Following MALDI-TOF-MS analyses were performed. Results In BxPC3 Akt Thr308 was phosphorylated by S100A8/A9, while in Capan1 and MiaPaCa2 PaCa cells lines. S100A8, S100A9, S100A8/A9 were incubated with equimolar concentrations of calcium and TGF-β1 for 24 h at 37°C. Following MALDI-TOF-MS analyses were performed. Results In BxPC3 Akt Thr308 was phosphorylated by S100A8/A9, while in Capan1 and MiaPaCa2 PaCa cells lines. S100A8, S100A9, S100A8/A9 were incubated with equimolar concentrations of calcium and TGF-β1 for 24 h at 37°C. Following MALDI-TOF-MS analyses were performed. Results

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Conclusion S100A8/A9 proteins in pancreatic cancer might favour cancer cell growth by inducing Akt, mTOR and NF-κB. In the less invasive BxPC3 cells S100A8 activates NF-κB. In more aggressive Capan1 and MiaPaCa2 cells S100A8, S100A9 and S100A8/A9 activate mainly Akt and mTORC1, not NF-κB pathways. TGF-β1 was demonstrated to be a new binding partner of S100A9 and this will open new fields of investigation on these interesting and complex inflammatory proteins in the PaCa setting.