Pituitary tumor fibroblast

Tumour-associated fibroblasts (TAFs) are key elements of the tumour microenvironment, but their role in pituitary neuroendocrine tumours (PitNETs) has been little explored. We hypothesised that TAF-derived cytokines may play a role in tumour aggressiveness, and that their release can be inhibited by somatostatin analogues. TAFs were isolated and cultured from 16 PitNETs (11 clinically non-functioning tumours and 5 somatotropinomas). The fibroblast secretome was assessed with a 42plex cytokine array before and after multiligand somatostatin receptor agonist pasireotide treatment. Angiogenesis and epithelial-to-mesenchymal transition pathway assessment included CD31, Ecadherin and ZEB1 expression. GH3 cells treated with TAF- or skin fibroblast-conditioned medium were assessed for migration, invasion and cell morphology changes. PitNET TAFs secreted significant amounts of cytokines including CCL2, CCL11, VEGF-A, CCL22, IL-6, FGF-2 and IL-8. TAFs from PitNETs with cavernous sinus invasion secreted more IL-6 levels compared to fibroblasts from non-invasive tumours (p=0.027). Higher CCL2 release from TAFs correlated with more capillaries (r=0.672, p=0.004), and TAFs from PitNETs with a higher Ki-67 tended to secrete more CCL2 (p=0.058). SST1 is the predominant somatostatin receptor in TAFs, and pasireotide decreased TAF-derived IL-6 by 80% (p<0.001) and CCL2 by 35% (p=0.038). GH3 cells treated with TAF-conditioned medium showed increased migration and invasion compared to cells treated with skin fibroblast-conditioned medium, with morphological and E-cadherin and ZEB1 expression changes suggesting epithelial-tomesenchymal transition. TAF-derived cytokines may increase PitNETs aggressiveness, alter angiogenesis and induce epithelial-to-mesenchymal transition changes. Pasireotide's inhibitory effect on TAF-derived cytokines suggest that this effect may play a role in its anti-tumour effects¹⁾.

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Marques P, Barry S, Carlsen E, Collier D, Ronaldson A, Awad S, Dorward N, Grieve J, Mendoza N, Muquit S, Grossman AB, Balkwill F, Korbonits M. Pituitary tumour fibroblast-derived cytokines influence tumour aggressiveness. Endocr Relat Cancer. 2019 Oct 1. pii: ERC-19-0327.R2. doi: 10.1530/ERC-19-0327. [Epub ahead of print] PubMed PMID: 31645017.

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