SSTR3 is a putative target for the medical treatment of gonadotroph adenomas of the pituitary.

Abstract:
Gonadotroph pituitary adenomas (GPAs) often present as invasive macroadenomas not amenable to complete surgical resection. Radiotherapy is the only post-operative option for patients with large invasive or recurrent lesions. No medical treatment is available for these patients. The somatostatin analogs (SSAs) octreotide and lanreotide that preferentially target somatostatin receptor type 2 (SSTR2) have little effect on GPAs. It is widely accepted that the expression of specific SSTR subtypes determines the response to SSAs. Given that previous studies on mRNA and protein expression of SSTRs in GPAs have generated conflicting results, we investigated the expression of SSTR2, SSTR3, and SSTR5 (the main targets of available SSAs) in a clinically and pathologically well-characterized cohort of 108 patients with GPAs. A total of 118 samples were examined by immunohistochemistry using validated and specific MABs. Matched primary and recurrent tissues were available for ten patients. The results obtained were validated in an independent cohort of 27 GPAs. We observed that SSTR3 was significantly more abundant than SSTR2 (P<0.0001) in GPAs, while full-length SSTR5 was only expressed in few tumors. Expression of SSTR3 was similar in primary and recurrent
adenomas, was high in potentially aggressive lesions, and did not change significantly in adenomas that recurred after irradiation. In conclusion, low levels of expression of SSTR2 may account for the limited response of GPAs to octreotide and lanreotide. Given the potent anti-proliferative, pro-apoptotic, and anti-angiogenic activities of SSTR3, targeting this receptor with a multireceptor ligand SSA such as pasireotide may be indicated for potentially aggressive GPAs.

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