STAT-Related Profiles Are Associated with Patient Response to Targeted Treatments in Locally Advanced SCCHN

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Source

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Abstract

The anti-epidermal growth factor receptor antibody cetuximab (Erbitux, CTX) is currently used for the treatment of locally advanced squamous cell carcinoma of the head and neck (LA-SCCHN), as yet with modest effectiveness, prompting for the identification of response predictors to this treatment and for the targeting of additional pathways implicated in this disease. Within this scope, we investigated the effect of SRC/STAT pathway components on LA-SCCHN patient outcome. SRC, STAT1, STAT3, STAT5A, STAT5B, ANXA1, CAV1, IGFBP2, EPHA2, EPHB2, and MSN relative gene expression, as well as Stat protein activation, were assessed on LA-SCCHN tumor tissues from 35 patients treated with combined radiotherapy (RT) and CTX-based regimens. Stat1, Stat3, and Stat5 proteins were usually found activated in neoplastic nuclei (70.4%, 85.7%, and 70.8%, respectively). Activated Stat3 and Stat5 were associated with each other (P = .017) and with a CAV1(high)/MSN(high)/IGFBP2(low) profile. All patients with tumors expressing high STAT5A/EPHA2 experienced a complete response on RT-CTX-based treatments (12/15 complete responders, P < .0001) and a longer progression-free survival (P = .024). Few tumors expressed high ANXA1/CAV1/EPHA2 and low IGFBP2, a putative dasatinib response-related profile, whereas high ANXA1 was associated with shorter overall survival (P = .003). In conclusion, Stat activation is common in LA-SCCHN, where overexpression of STAT5A and EPHA2 may predict for response to RT-CTX treatments. The STAT5A/EPHA2 profile seems of particular interest for validation in larger cohorts and in multiple tumor types because markers for the positive selection of patients to benefit from CTX-containing treatments are currently lacking.