阿部　信　先生の論文がPathology International（IF 3.4)に受理されました。

本研究は、脂肪分化の制御に関与するSETD5遺伝子に着目したものです。良性・悪性を含む脂肪性腫瘍100例を対象にSETD5の免疫組織化学的発現を系統的に評価した結果、SETD5の発現は良性腫瘍から悪性腫瘍（肉腫）へ進むにつれて高まる傾向が示されました。脱分化脂肪肉腫においては、脱分化成分でSETD5発現の亢進がみられ、特に高発現群で全生存期間（OS）短縮との関連が示唆されました。今後、境界病変の補助診断や予後層別化モデルへの統合が期待されます。（阿部）

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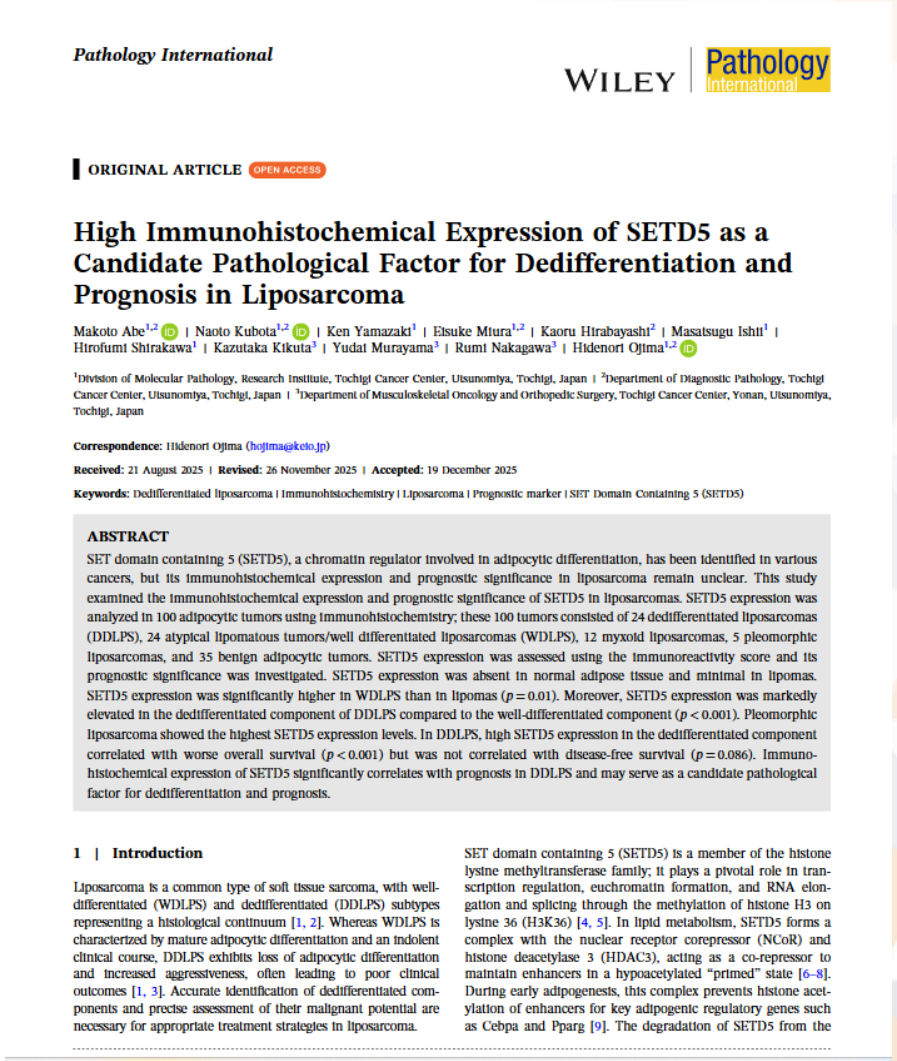

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High Immunohistochemical Expression of SETD5 as a Candidate Pathological Factor for Dedifferentiation and Prognosis in Liposarcoma

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ABSTRACT

SET domain containing 5 (SETD5), a chromatin regulator involved in adipocytic differentiation, has been identified in various cancers, but its immunohistochemical expression and prognostic significance in liposarcoma remain unclear. This study examined the immunohistochemical expression and prognostic significance of SETD5 in liposarcomas. SETD5 expression was analyzed in 100 adipocytic tumors using immunohistochemistry; these 100 tumors consisted of 24 dedifferentiated liposarcomas (DDLPS), 24 atypical lipomatous tumors/well differentiated liposarcomas (WDLPS), 12 myxoid liposarcomas, 5 pleomorphic liposarcomas, and 35 benign adipocytic tumors. SETD5 expression was assessed using the immunoreactivity score and its prognostic significance was investigated. SETD5 expression was absent in normal adipose tissue and minimal in lipomas. SETD5 expression was significantly higher in WDLPS than in lipomas ($p = 0.01$). Moreover, SETD5 expression was markedly elevated in the dedifferentiated component of DDLPS compared to the well-differentiated component ($p < 0.001$). Pleomorphic liposarcoma showed the highest SETD5 expression levels. In DDLPS, high SETD5 expression in the dedifferentiated component correlated with worse overall survival ($p < 0.001$) but was not correlated with disease-free survival ($p = 0.086$). Immunohistochemical expression of SETD5 significantly correlates with prognosis in DDLPS and may serve as a candidate pathological factor for dedifferentiation and prognosis.

1 | Introduction

Liposarcoma is a common type of soft tissue sarcoma, with well-differentiated (WDLPS) and dedifferentiated (DDLPS) subtypes representing a histological continuum [1, 2]. Whereas WDLPS is characterized by mature adipocytic differentiation and an indolent clinical course, DDLPS exhibits loss of adipocytic differentiation and increased aggressiveness, often leading to poor clinical outcomes [1, 3]. Accurate identification of dedifferentiated components and precise assessment of their malignant potential are necessary for appropriate treatment strategies in liposarcoma.

SET domain containing 5 (SETD5) is a member of the histone lysine methyltransferase family; it plays a pivotal role in transcription regulation, euchromatin formation, and RNA elongation and splicing through the methylation of histone H3 on lysine 36 (H3K36) [4, 5]. In lipid metabolism, SETD5 forms a complex with the nuclear receptor corepressor (NCoR) and histone deacetylase 3 (HDAC3), acting as a co-repressor to maintain enhancers in a hypoacetylated "primed" state [6–8]. During early adipogenesis, this complex prevents histone acetylation of enhancers for key adipogenic regulatory genes such as Cebpa and Pparg [9]. The degradation of SETD5 from the