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Review article

An Updated Conceptual Framework for Myoepithelial Tumors of Soft tissues and Bone: Toward a Molecularly Informed Classification

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ABSTRACT

Myoepithelial tumors (MET) of soft tissue and bone comprise a rare group of neoplasms unified by partially overlapping morphology and so called myoepithelial immunophenotype. Historically, MET have long posed diagnostic and prognostic challenges. Grading and risk stratification have relied largely on the presence of cytologic atypia. Recent molecular and epigenetic studies have fundamentally revised this concept, demonstrating that MET represent a biologically heterogeneous family rather than a single disease entity. Soft tissue (mostly deep-seated) and osseous MET frequently harbor recurrent gene fusions, most commonly involving FET family genes (*EWSR1* or less often *FUS*) with partners such as *POU5F1, PBX1, PBX3, KLF15, KLF17*, and *ZNF444*, and more rarely non-FET fusions including *SS18::POU5F1*. These fusion types correlate with reproducible clinicopathologic patterns and, in emerging outcome datasets, with subtype-specific differences in behavior. In contrast, superficially located adnexal tumors with ductal differentiation - representing true cutaneous mixed tumors/myoepitheliomas - typically lack *EWSR1/FUS* rearrangements and instead show *PLAG1* rearrangements, supporting a *bona fide* myoepithelial origin and close relationship to *PLAG1*-driven salivary gland counterparts. Additional complexity arises from SMARCB1-deficient, fusion-negative tumors and a small subset lacking identifiable recurrent drivers, as well as substantial overlap in morphology and immunophenotype with multiple MET mimics, contributing to diagnostic misclassification when using morphology and immunohistochemistry alone. To address these issues, we synthesize clinicopathologic, molecular, methylomic and pooled outcome data across major MET subgroups from recent multi-institutional cohorts, highlighting pronounced epigenetic and clinical heterogeneity and providing practical diagnostic guidance for surgical pathologists. We propose a molecularly informed classification framework that improves diagnostic precision, clarifies terminology - particularly distinguishing *PLAG1*-rearranged cutaneous salivary-gland analogs from fusion-associated soft tissue/bone sarcomas with myoepithelial-like phenotype - and lays a foundation for refined prognostic stratification and future therapeutic studies.

Historical perspective

The contemporary concept of myoepithelial tumors (MET) of the skin, soft tissue, and bone—including mixed tumor, myoepithelioma, and myoepithelial carcinoma—was established in 1997 by Kilpatrick and Fletcher, who defined their characteristic morphologic and immunohistochemical features [1]. Morphologically, MET display trabecular, reticular, nested, and/or solid growth patterns composed of spindled to epithelioid cells embedded in myxoid, chondromyxoid, or hyalinized stroma, with mixed tumors often showing ductal differentiation. Immunohistochemically, MET are defined by co-expression of epithelial markers (broad-spectrum cytokeratins (CK) and/or EMA) and myoepithelial markers, most commonly S100 protein, SOX10, or GFAP [2].

Historically, the distinction between benign and malignant MET has relied largely on cytologic atypia. Tumors with absent or mild atypia generally behave in an indolent manner, whereas those with moderate to severe atypia (nuclear enlargement and hyperchromasia)—typically accompanied by increased mitotic activity—exhibit metastatic potential in approximately one-third-of cases [3].

A major advance occurred in 2010, when systematic molecular

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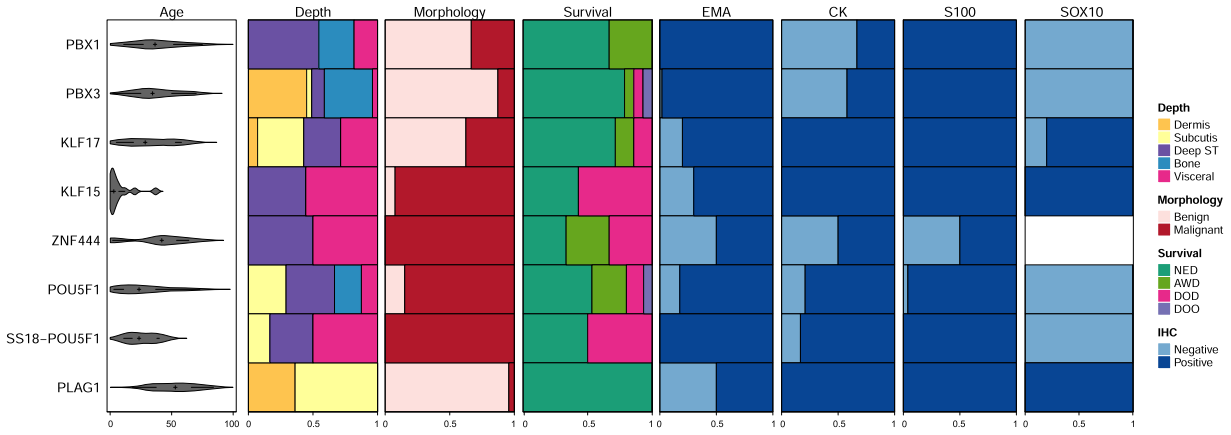

Fig. 1. Molecular subgroups of METs and their clinicopathologic associations. Stacked bar plots illustrating the distribution of clinical and pathologic features across fusion-positive MET molecular subgroups, including age, depth, tumor morphology (benign vs. malignant), survival status and comparison of IHC marker expression (EMA, CK, S100, SOX10) across molecular subgroups. White/blank denotes missing data. ST, soft tissues. NED, no evidence of disease, AWD, alive with disease, DOD, died of disease, DOO, died of other causes.

studies by Antonescu et al. demonstrated that a substantial subset of deep-seated soft tissue and osseous MET harbor *EWSR1* rearrangements with partners including *POU5F1, PBX1*, and *ZNF444* [4]. Subsequent work expanded the spectrum of *EWSR1* fusions to include *KLF15, KLF17*, and *PBX3*, and established correlations between specific fusion types and distinct morphologic patterns [5–8]. Less commonly, MET harbor *FUS* rearrangements [5] or alternative fusions such as *SS18::POU5F1* [9–12].

In contrast, superficially located tumors—typically benign and exhibiting ductal differentiation consistent with adnexal mixed tumors—generally *lack EWSR1* rearrangements (with the exception of so-called syncytial myoepitheliomas discussed later) and instead harbor *PLAG1* gene fusions [13–15]. The molecular landscape of MET has been further complicated by the identification of SMARCB1 loss in a subset of fusion-negative cases [16], the existence of tumors lacking identifiable recurrent molecular alterations [17,18], and overlap in terminology with salivary gland myoepithelial neoplasms of the head and neck [19].

Collectively, these findings indicate that MET, despite shared morphologic and immunophenotypic features, represent a biologically heterogeneous group. Notably, all systematic outcome studies predate the molecular era, leaving the prognostic significance of individual molecular subtypes uncertain.

To address these issues, we recently conducted a multi-institutional study of soft tissue and bone MET, including 53 newly identified fusion-positive cases representing the most common rearrangements. We also performed a pooled clinicopathologic analysis incorporating these cases with all 130 previously reported molecularly confirmed MET, with particular emphasis on clinical outcome. In parallel, DNA methylation profiling of 52 MET across all major molecular subgroups was performed to assess epigenetic relatedness among MET and to salivary gland counterparts. This integrated approach revealed pronounced clinicopathologic and epigenetic heterogeneity, including substantial differences in biological behavior across molecular subtypes [20], findings corroborated by recent independent epigenetic and transcriptomic studies [17,21].

This review highlights the key advances most relevant to practicing surgical pathologists and proposes a framework for a molecularly informed classification of myoepithelial tumors of soft tissue and bone with important diagnostic and clinical implications.

MET is not a single disease: toward a molecular classification of soft tissue and bone MET

Current MET classification relies on MET-compatible morphology plus a "myoepithelial" immunophenotype—epithelial marker expression (CK and/or EMA) coupled with S100, SOX10, or GFAP. While inexpensive and widely applicable, this approach has major limitations. First, it lacks specificity: Malik et al. showed that tumors meeting morphologic/IHC "MET-spectrum" criteria may instead harbor defining alterations of other entities (e.g., extraskeletal myxoid chondrosarcoma, synovial sarcoma, ossifying fibromyxoid tumor), with a misclassification rate >20% even after expert review [17]. Second, sensitivity is imperfect: ~10% of fusion-confirmed MET lack expression of all canonical myoepithelial markers [8,20]. Third, predicting behavior remains difficult. Although Hornick and Fletcher's criteria broadly separate benign from malignant [3], their application is subjective and may be less reproducible outside specialized consultation practice. Finally, and most importantly, the current framework merges clinicopathologically and epigenetically diverse neoplasms. Recent molecular/epigenetic work demonstrates substantial subtype-specific differences in morphology, immunophenotype, outcome, and potentially therapeutic vulnerabilities [8,17,.20,21].

Accordingly, MET are best viewed as a family of diverse but phenotypically overlapping neoplasms—analogous to e.g. round cell sarcomas or, to a degree, rhabdomyosarcomas or liposarcomas, rather than a single entity. We therefore outline a primarily molecular-centric classification that should improve diagnostic precision and prognostic stratification. While molecular testing is often required for definitive assignment, a meaningful subset can be predicted with reasonable confidence using morphology and IHC only.

MET subtypes based on molecular and epigenetic features

Multiple unsupervised dimensionality reduction and clustering analyses based on transcriptomic and/or methylomic profiling confirm marked MET heterogeneity [17,20–23]. It has long been proposed that myoepithelial neoplasms of the skin and soft tissue represent analogs of salivary gland myoepithelial tumors [13,14]. However, accumulating molecular and epigenetic evidence indicates that this concept should be restricted to *PLAG1*-altered cutaneous myoepitheliomas. Across studies, *PLAG1*-rearranged cutaneous myoepitheliomas overlap epigenetically with *PLAG1*-altered salivary gland myoepithelial neoplasms (pleomorphic adenoma and related tumors), and are distinct from the entire group of FET (*EWSR1/FUS*)-rearranged soft tissue/bone MET [17,20,21,23].

Within FET-rearranged tumors, methylomes are more similar to one another than to most other mesenchymal entities, yet they tend to segregate by fusion-defined subgroup. Together with clinicopathologic differences, these findings argue against viewing FET-rearranged MET as a single myoepithelial entity with variable FET fusions and instead

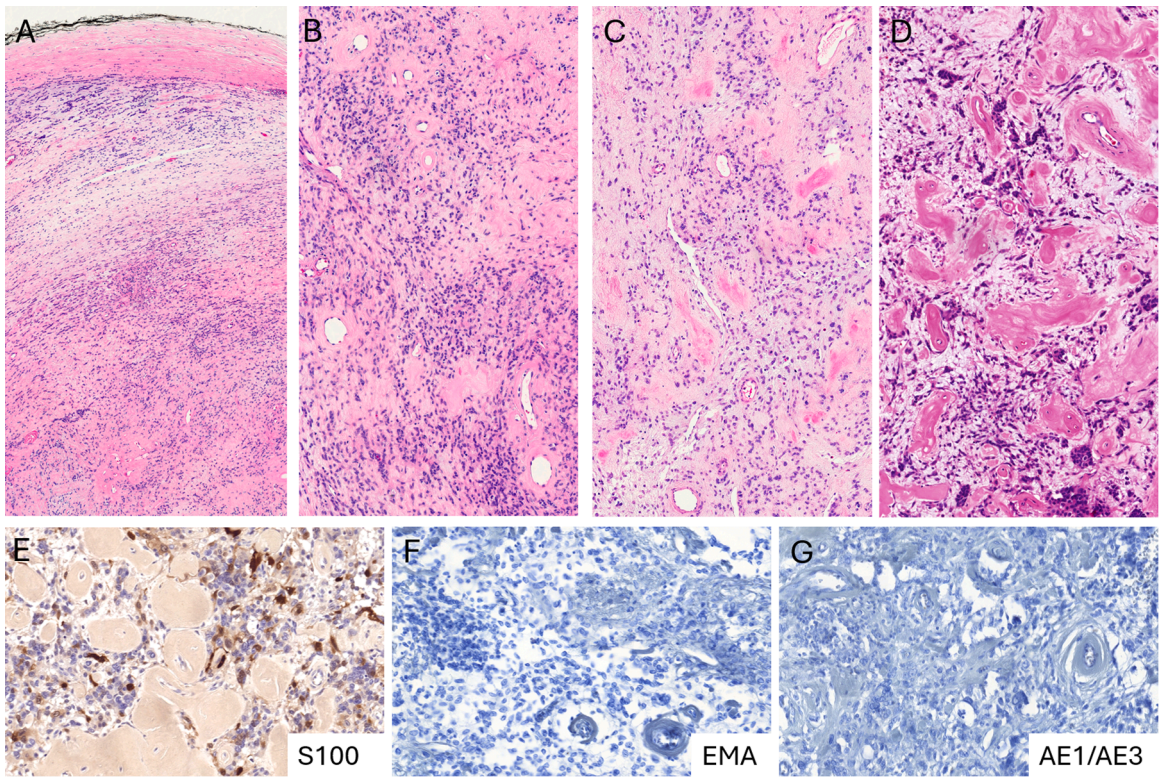

Fig. 2. ***EWSR1/FUS::POU5F1*** **tumors at the benign end of the morphological spectrum.** Tumors are hypocellular and composed of spindled to epithelioid cells embedded in abundant collagenized stroma, frequently with prominent perivascular and stromal hyalinization that may mimic kinase fusion–associated neoplasms (**A–D**). Three representative cases are shown, with panels A and B illustrating the same tumor. Immunohistochemically, most tumors express S100 protein, AE1/AE3, and EMA; however, staining is often focal or patchy (**E**, S100 protein) and may rarely be entirely absent (**F**, EMA; **G**, AE1/AE3). Panels D–F depict immunohistochemical findings in the same case illustrated in panels A and B.

support their classification as a family of fusion-associated sarcomas unified by a myoepithelial-like phenotype rather than true myoepithelial differentiation [20].

Recent methylation analyses also included SMARCB1-deficient tumors. Upon unsupervised dimensionality reduction and clustering analyses, they clustered with epithelioid sarcoma rather than with other MET [17,20], consistent with the strong epigenetic effects of SWI/SNF alterations and possible biologic relatedness [24].

Accordingly, we suggest dividing soft tissue and bone MET into fusion-positive and fusion-negative categories. Fusion-positive MET comprise: (i) FET-rearranged tumors including *EWSR1::POU5F1, EWSR1::KLF15, EWSR1/FUS::KLF17, EWSR1::ZNF444*, and *EWSR1::PBX1/PBX3*; and (ii) non-FET fusions, currently consists mostly of *SS18::POU5F1* and potentially other emerging entities. A separate, primarily cutaneous MET category is defined by *PLAG1* fusions (adnexal mixed tumors/myoepitheliomas). Fusion-negative MET include SMARCB1-deficient tumors and cases with currently unknown drivers.

Fusion-positive MET

This section provides an overview of the clinicopathological features of all previously reported molecularly confirmed fusion-positive MET analyzed in our recent study; detailed clinicopathologic and outcome comparative analyses are provided therein [20]. Key clinicopathological features are also summarized in Fig. 1. As discussed in the preceding section, and notwithstanding prevailing terminology, FET-rearranged "MET" are best regarded as fusion-associated sarcomas with a myoepithelial-like phenotype rather than true myoepithelial-derived neoplasms [20]. A recurrent feature of these tumors is their frequent tendency toward morphological progression from benign or low-grade-appearing lesions to poorly differentiated, monomorphic neoplasms, paralleling the behavior observed in other fusion-associated sarcomas, including *EWSR1::PATZ1*-rearranged sarcomas [25,26], kinase-altered spindle cell neoplasms [27,28] or myxoid liposarcomas.

FET-rearranged MET

EWSR1/FUS::POU5F1 group (number of reported cases=33). ***EWSR1::POU5F1*** (rarely *FUS::POU5F1*) tumors occur mainly in children and young adults (median 26 years) and show a predilection for the extremities, with occasional renal, osseous, and truncal presentations. Most are malignant, spanning a morphologic continuum. At the benign end of the spectrum, tumors are hypocellular and composed of spindled to epithelioid cells embedded in abundant collagenized stroma, often with prominent perivascular and stromal hyalinization that may mimic kinase-altered spindle cell neoplasms (Fig. 2A-D). The most common ("intermediate") pattern is characterized by solid sheets and nests of large epithelioid cells with clear cytoplasm (Fig. 3A-B). Along this continuum, the amount of clear cytoplasm may progressively diminish (Fig. 3C), culminating in areas with an undifferentiated round cell morphology. In high-grade examples, undifferentiated round cell sarcoma may predominate, occasionally retaining focal areas with residual clear cell features (Fig. 3D), while some cases are composed entirely of undifferentiated round cells (Fig. 3E-F).

Mitotic activity ranges from 0 to 20/10 HPF (median 2); necrosis occurs in ¼ of cases. Most express S100 (Fig. 2E), CK, EMA, and, with variable GFAP, and are typically negative for SOX10 and p63. Rare cases were EMA (Fig. 2F) and/or CK (Fig. 2G) negative. Clinically, these are aggressive neoplasms, with metastases in ~50% [4,8,17,18,20,29–31].

EWSR1/FUS::KLF17 group (n = 16). ***KLF17***-rearranged tumors (*FUS::KLF17* in ~2/3; *EWSR1::KLF17* in the remainder) occur mainly in young

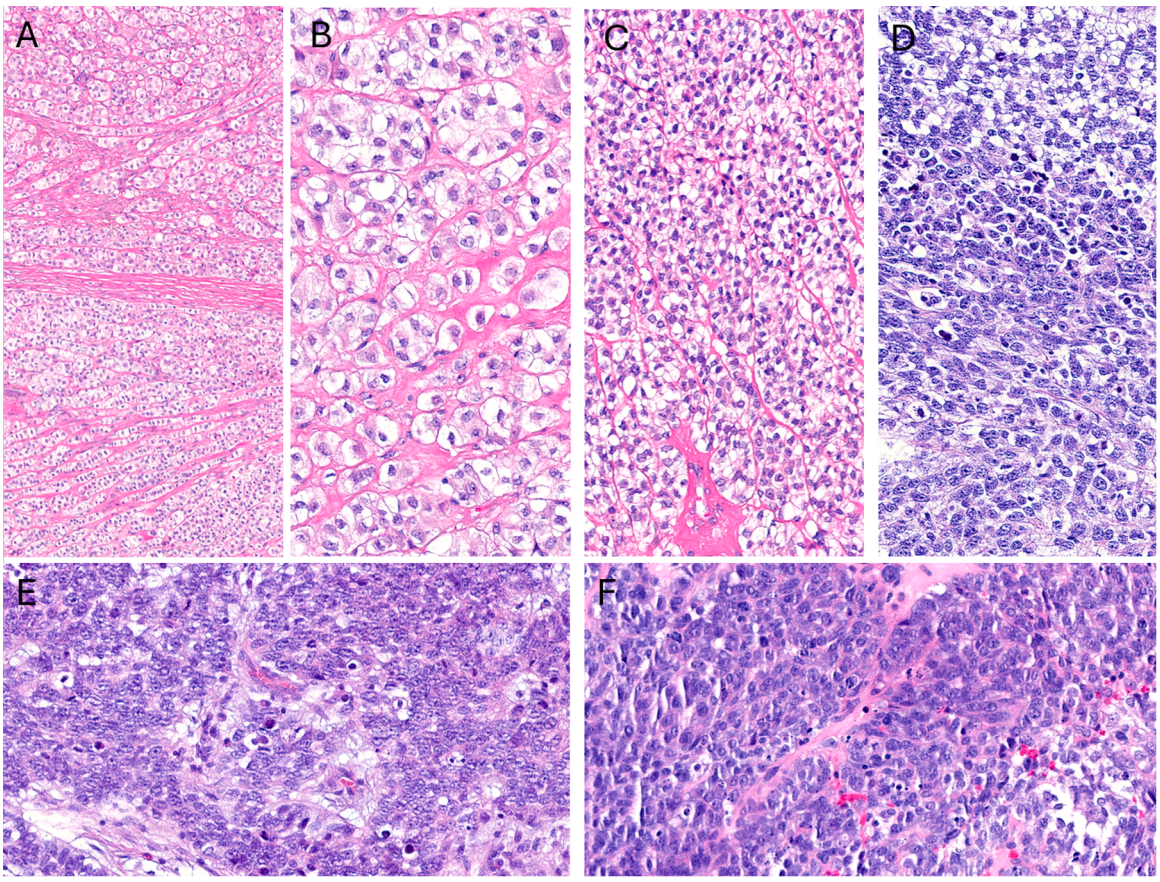

Fig. 3. *EWSR1/FUS::POU5F1* tumors at the intermediate to high-grade end of the morphological spectrum. The most common pattern consists of sheets and nests of large epithelioid cells with clear cytoplasm (**A, B**). Along the morphological continuum, the amount of clear cytoplasm may progressively diminish, as illustrated in panel **C** (same case as panels A and B), with transition to an undifferentiated round cell morphology. High-grade examples may show predominant undifferentiated round cell sarcoma, occasionally retaining focal areas with residual clear cell features (**D, E**; same case). Some cases are composed entirely of undifferentiated round cells (**F**).

adults (median 29 years), usually affect the lower extremity and visceral sites (especially pleura/lung), and show no clear differences by 5′ fusion gene partner. These neoplasms display a characteristic trabecular or corded growth pattern set within a myxohyaline stroma, again forming a morphological continuum. At the benign end of the spectrum (approximately two-thirds of the cases), lesions are hypocellular and composed of bland spindled to epithelioid cells arranged in delicate cords and trabeculae (Fig. 4A, D, F). More commonly, tumors exhibit moderately increased cellularity and, in some cases, increased cytologic atypia, while retaining the same architectural framework and closely resembling parachordoma (Fig. 4B, E, G, H) [32]. Rare cases progress to an undifferentiated small round/epithelioid cell morphology (Fig. 4C). Mitotic activity ranges from 0 to 18/10 HPF (median 0); necrosis is rarely present. All tested cases express S100 and CK; most also express EMA and SOX10 (Fig. 4E – inset). Clinically, 3/8 metastasized and 1 patient died of disease [5,8,18,20,33].

EWSR1::KLF15 group (n = 13). *EWSR1::KLF15* tumors show a striking predilection for infants and young children (median 3 years; typically <5 years) and usually involve extremities or viscera. Reported tumors have uniformly malignant histology, most often sheets/cords of undifferentiated round-to-spindled cells in myxoid stroma (Fig. 5A-C). Mitotic activity ranges from 2 to >5/10 HPF; necrosis is present in most cases. All tested cases were S100, SOX10, and CK positive; most also expressed EMA and GFAP. Outcomes are poor: ~two-thirds metastasize and nearly half of patients die of disease [7,8,17,20,34–37].

EWSR1::ZNF444 group (n = 4). Only four *EWSR1::ZNF444* cases have been reported to date. All patients were female, spanning a broad age range; sites included head (n = 2), pleura/lung (n = 1), and thigh (n = 1). All were malignant, composed of poorly differentiated round/epithelioid cells in fibrous or fibromyxoid stroma (Fig. 6A-C). Mitotic rates (reported in two cases) were 5 and 30/10 HPF; necrosis was present in 1/3 evaluable cases. CK, EMA, and S100 were positive in 2/4; both tested cases were GFAP positive. Two of three cases had aggressive clinical courses [8,20,38].

EWSR1::PBX1/PBX3 group (n = 67). *PBX1/PBX3*-rearranged tumors arise most often in skin (and less commonly deep soft tissue), or in long bones; a minority occur in thoracic visceral sites. They affect mainly young-to-middle-aged adults (median 35 years) and are uncommon in children. Cutaneous cases—typically diagnosed as syncytial myoepithelioma [39] —are likely underrecognized and, anecdotally, among the most frequent “MET” encountered in routine/consultation practice.

Morphologically, most cases (particularly cutaneous lesions) are benign-appearing syncytial myoepitheliomas: solid, sheet-like growth of uniform ovoid-to-spindle cells, low mitotic activity, and no necrosis (Fig. 7A-B). A helpful clue is a frequent perivascular lymphocytic infiltrate (Fig. 7B) [39,40]. A minority, especially in bone, show malignant cellular round-to-spindle morphology (Fig. 7E-F) with increased mitotic activity and occasional necrosis [41]; some retain areas of bland syncytial morphology, supporting progression. Immunophenotypically, nearly all are S100 (Fig. 7C) and EMA (Fig. 7D) positive; CK is positive in <50%. SOX10 is consistently negative, while occasional weak GFAP expression has been reported in non–molecularly confirmed cases [39].

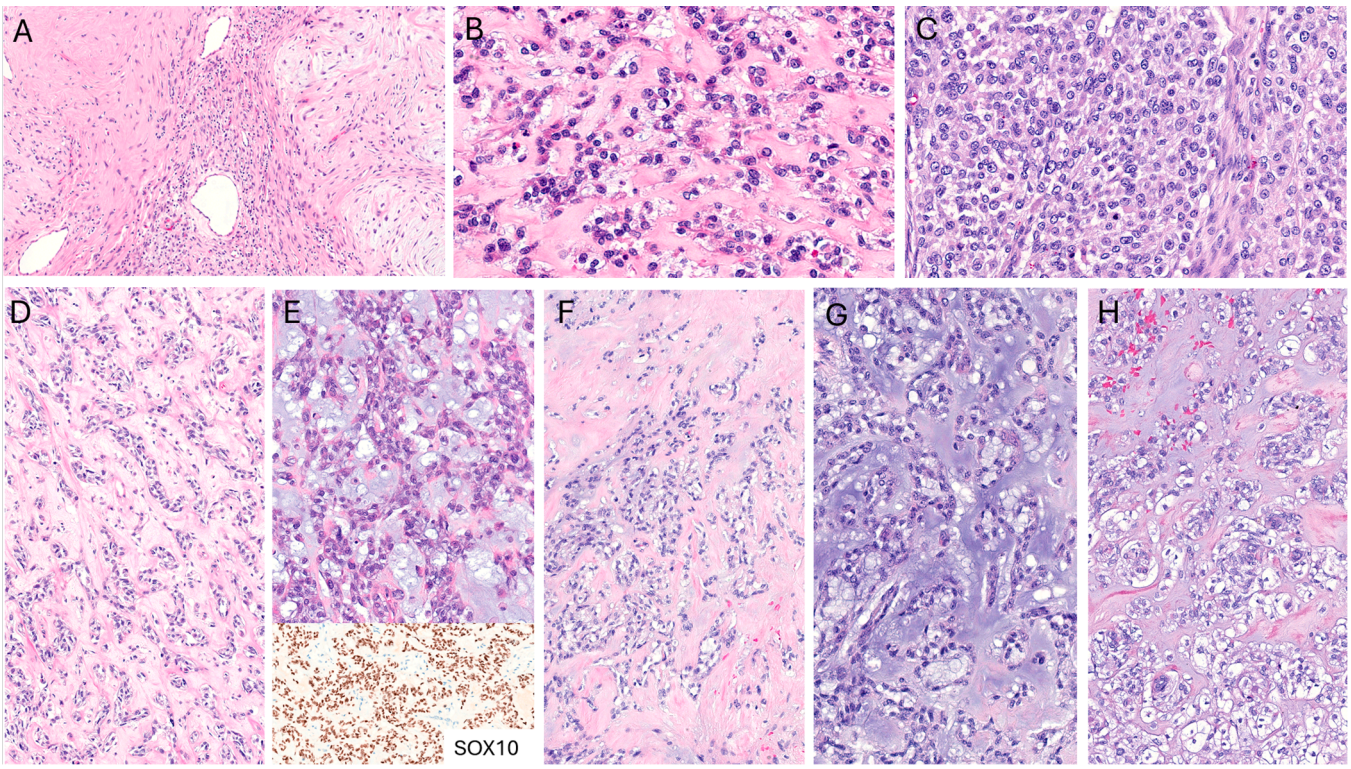

Fig. 4. Morphological spectrum of tumors harboring *EWSR1/FUS::KLF17* fusion. The benign end of the spectrum is characterized by hypocellular proliferations of bland spindled to epithelioid cells arranged in trabecular/corded patterns within a myxohyaline stroma (**A, D, F**). More commonly, tumors retain the trabecular/corded architecture within a myxohyaline stroma but show increased cellularity and cytologic atypia, closely resembling parachordoma (**B, E, G, H**). Rarely, progression to an undifferentiated small round/epithelioid cell morphology is observed (**C**). Panels A–C, D–E, and F–H illustrate four different cases. In contrast to other FET-rearranged myoepithelial tumors, the *EWSR1/FUS::KLF17* (and *EWSR1::KLF15*) fusion subset consistently exhibits near-uniform SOX10 expression (**inset in panel E**).

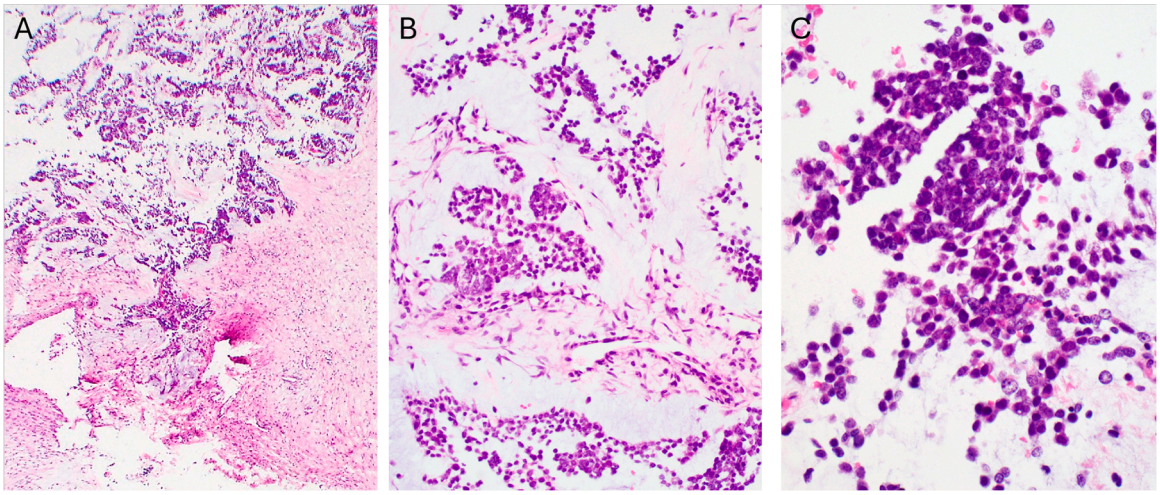

Fig. 5. EWSR1::KLF15 tumors. These neoplasms are typically composed of undifferentiated round to spindled cells embedded in a myxoid to fibromyxoid stroma (**A–C**).

Molecularly, ~80% harbor *EWSR1::PBX3* and the remainder *EWSR1::PBX1*, without major phenotypic differences between the two groups. Follow-up for molecularly confirmed cutaneous cases is limited, but morphologic series suggest benign syncytial myoepithelioma rarely recurs, even if incompletely excised [39,40,42]. In contrast, osseous cases show higher recurrence risk and, in malignant examples, metastatic potential and occasional disease-specific death [4,6,8,17,20,40,42–46].

MET with non-FET fusions

SS18::POU5F1 group (n = 6). *SS18::POU5F1* tumors affect adolescents/young adults (median 23.5 years) and, unlike *EWSR1/FUS::POU5F1*, have thus far spared the extremities, arising in groin, back, viscera, and parotid gland. All reported cases were malignant, composed of sheets/nests of high-grade undifferentiated epithelioid-to-round cells with brisk mitotic activity and frequent necrosis (Fig. 6D); one showed ganglioneuromatous differentiation [47]. All expressed EMA and S100; most

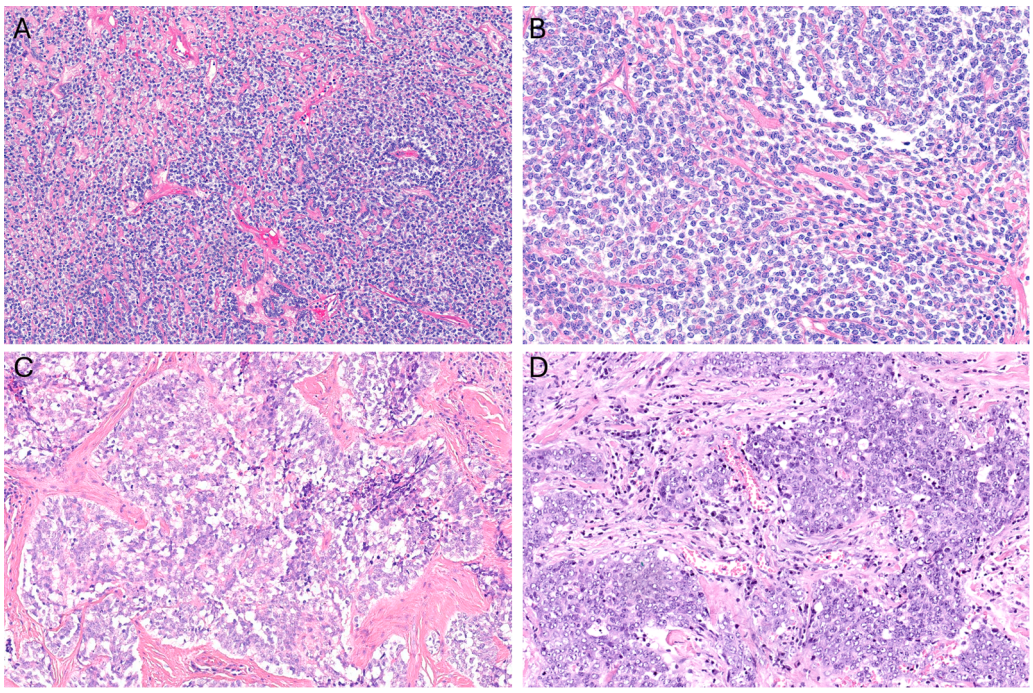

Fig. 6. EWSR1::ZNF444 and SS18::POU5F1 tumors. EWSR1::ZNF444 neoplasms are composed of poorly differentiated round to epithelioid cells set within a fibrous to fibromyxoid stroma (**A–C**). Panels A and B illustrate the same case, while panel C shows a separate tumor with the same fusion. Similarly, tumors harboring *SS18::POU5F1* consist of solid sheets or nests of undifferentiated round to epithelioid cells (**D**).

also CK; all tested were SOX10 and p63 negative. Prior RNA-seq clustering placed *SS18::POU5F1* tumors with *EWSR1/FUS::POU5F1* cases [9], and our methylation data similarly aligned a case of *SS18::POU5F1* MET with the *POU5F1*-rearranged FET group [20]. Despite limited follow-up, outcomes of *SS18::POU5F1* MET appeared worse than in *EWSR1/FUS::POU5F1* tumors (5/6 metastasized; 2/4 died of disease) [9–12,20,47]. Larger series are needed to determine whether this represents a molecular variant within the broader *POU5F1*-rearranged group or a distinct subset.

PLAG1-rearranged apocrine mixed tumors/myoepitheliomas of the skin adnexa (n = 47). These neoplasms have been variably termed mixed tumor (chondroid syringoma) or MET, spanning epithelial-predominant apocrine mixed tumors [15,21,48] to myoepithelial-predominant/hyaline cell–rich lesions usually labeled as myoepitheliomas or MET [15,49]. For practical and conceptual consistency, we separate these categories using a threshold of <5% ductal differentiation, in line with recent studies [15,41].

The highly concordant morphology, immunophenotype, and genotype, and—as discussed above—epigenetic profiles, strongly support the classification of *PLAG1*-altered cutaneous tumors as true analogs of salivary gland myoepithelial neoplasms [13–15]. This relationship is biologically plausible given their anatomic proximity to cutaneous apocrine-type sweat glands, which share overlapping histologic features with salivary glands, including the presence of a *bona fide* myoepithelial cell layer co-expressing CK, SOX10, and S100 protein [14,21]. This concept is further reinforced by the fact that most salivary gland pleomorphic adenomas are likewise driven by *PLAG1* rearrangements [22]. In contrast, myoepithelial neoplasms of deep soft tissue and bone do not display similar association with non-neoplastic myoepithelial cells and their immature precursors within sweat glands. Further, they typically do not harbor *PLAG1* alterations and are instead usually associated with FET fusions [20].

Compared with FET-rearranged soft tissue MET, *PLAG1*-altered cutaneous myoepitheliomas occur in older patients (median 53 years; none <18 years in our 47-case cohort) and arise in skin/subcutis, most often on acral extremities or the face. With rare exceptions (2 cases), they are histologically benign, presenting as well-circumscribed dermal/subcutaneous nodules of epithelioid/plasmacytoid cells in myxoid stroma (Fig. 8A-C), often with minor ductal structures (<5%; Fig. 8C) and/or hyaline cartilage (Fig. 8D). Atypia is absent/mild; mitotic activity ranges 0–8/10 HPF (median 0); small necrosis foci (1–5%) may be present. Importantly, ductal differentiation and cartilage—common here—are absent across other fusion-positive MET subgroups. Immunohistochemically, *PLAG1*-altered tumors show co-expression of CK (Fig. 8E), S100 (Fig. 8F), and SOX10 (Fig. 8G) with virtually all tumor cells showing strong staining, a pattern usually not seen in other fusion-positive MET. EMA and GFAP are positive in ~half and p63 in ~two-thirds of *PLAG1*-altered tumors (whereas most FET-rearranged cases are p63 negative). PLAG1 IHC is positive in all 14 tested cases (Fig. 8H). Although its specificity has not yet been systematically evaluated, strong and diffuse nuclear PLAG1 expression by IHC appears to be a useful supportive diagnostic marker in the appropriate clinicopathologic context. At the molecular level, these tumors are characterized by rearrangements of the *PLAG1* gene with a variety of fusion partners, most commonly *TRPS1* and *LIFR* [20]. Similar to salivary gland myoepithelial neoplasms, rare cutaneous apocrine mixed tumors have been reported to harbor *HMGA2* rearrangements [15,21]; however, to date, *HMGA2* rearrangements have not been described in the myoepithelial-predominant (i.e., cutaneous myoepithelioma) variant. Available outcome data confirm predominantly benign behavior, with metastasis documented in only one of 11 patients and a median follow-up of 96 months [13–15,41,43].

Other potential MET fusions

As broader NGS panels and whole-transcriptome assays are increasingly being used in clinical practice, additional fusions will likely be identified among MET previously lacking known drivers, particularly involving genes not covered by older targeted panels with limited gene coverage. Malik et al., for example, reported an *IRF2BP2::CDX1* fusion in tumors histologically consistent with MET [17].

In addition, two methylation studies reported overlap between methylomes of *FET::NFATC2* sarcomas and FET-rearranged MET [17,

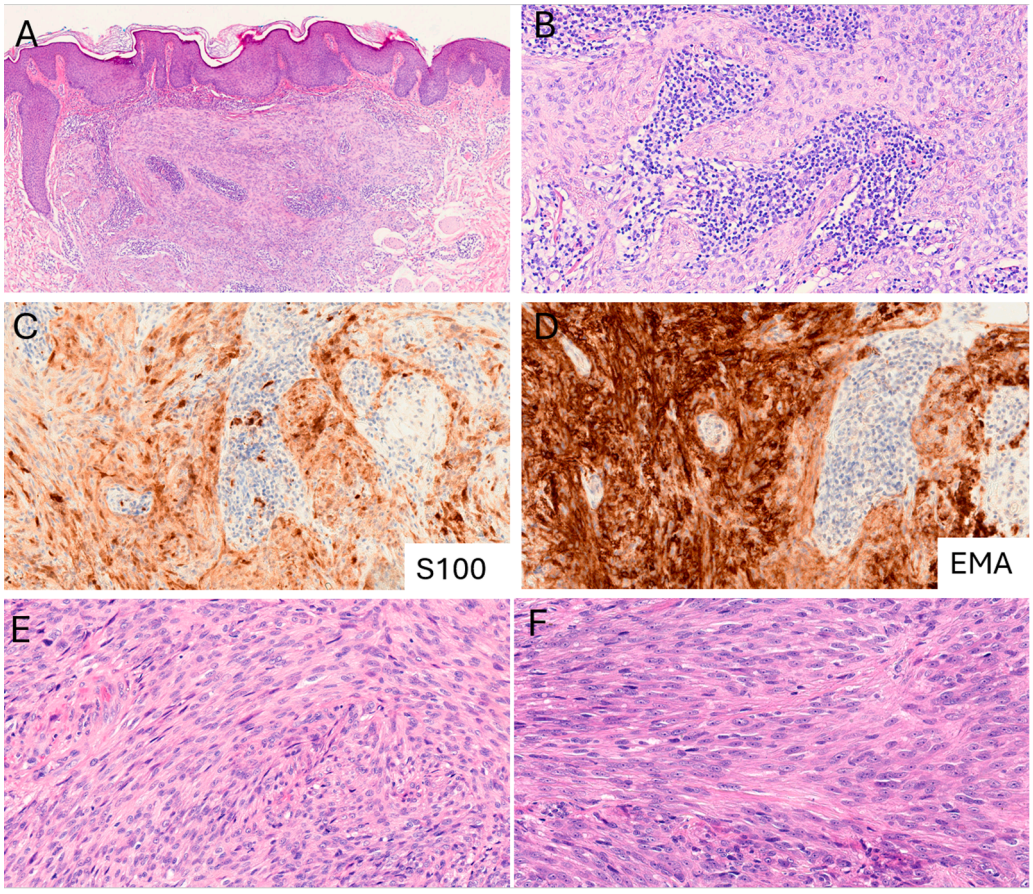

Fig. 7. Morphological spectrum of tumors harboring *EWSR1:PBX1/3*. Benign tumors exhibit a characteristic syncytial myoepithelioma morphology, composed of solid, sheet-like proliferations of uniform ovoid/spindle cells with low mitotic activity, and absence of necrosis (**A, B**). A helpful clue is a frequent perivascular lymphocytic infiltrate (**B**). Immunohistochemically, these tumors show consistent expression of S100 protein (**C**) and EMA (**D**), whereas only a minority of cases demonstrate positivity for AE1/AE3 (not shown). Although most tumors are benign, rare cases - particularly those arising in bone or visceral sites - may progress to hypercellular neoplasms with round-to-spindle cell morphology, increased cytologic atypia, elevated mitotic activity, and occasional necrosis (**E, F**).

20]. The former is currently classified among undifferentiated round cell sarcomas in the World Health Organization (WHO) Classification of Soft Tissue and Bone Tumors [50]). Given their MET-like morphology, variable EMA/CK expression, and presence of FET fusions [51], *NFAT-C2*-rearranged sarcomas may ultimately be more appropriately grouped with MET, pending further investigations [20]. On the other hand, other potential phenotypic mimics, e.g., extraskeletal myxoid chondrosarcoma and ossifying fibromyxoid tumor, do not show epigenetic overlap with MET [17,20].

Fusion-negative MET

Fusion-negative MET comprise SMARCB1-deficient tumors and cases with as yet unknown molecular drivers.

SMARCB1-deficient MET

Across MET cohorts, SMARCB1 loss is reported in ~10% of adult [52] and ~40% of pediatric MET [53], but to date there are no dedicated studies of SMARCB1-deficient MET. Interpretation is further complicated because SMARCB1 loss also occurs in other epithelial marker–positive neoplasms (epithelioid sarcoma, poorly differentiated chordoma, extrarenal rhabdoid tumor), and some may show S100 expression. Brachyury helps exclude poorly differentiated chordoma, whereas distinction from extrarenal rhabdoid tumor—particularly in children—may be challenging and sometimes arbitrary.

An additional emerging group includes SMARCB1-deficient vulvar tumors, previously termed "myoepithelioid tumor" or "myoepithelioma-like tumor" of the vulvar region [54–56]. Given their apparent anatomic restriction (female vulvar/groin; rare paratesticular cases [57,58]) and incomplete myoepithelial phenotype, it remains unclear whether they represent a variant of SMARCB1-deficient MET or a distinct genital soft tissue entity. Notably, despite substantial follow-up, reported cases have shown uniformly benign behavior [54–58], contrasting with the more aggressive SMARCB1-deficient MET summarized below.

Based on 15 reported SMARCB1-deficient MET identified in six studies, most have been malignant, with male predominance (~3:1) and a broad age range (1–68 years; median 22). Sites are diverse, most commonly lower extremity (n = 6), upper extremity (n = 5), viscera (n = 3), and head/neck (n = 1). Among cases with follow-up (n = 5), outcomes included disease-free (n = 2), alive with disease (n = 2), and died of disease (n = 2). Histology commonly shows solid sheets (less often cords/trabeculae) of epithelioid/rhabdoid cells, often in myxoid stroma. When detailed, tumors were consistently EMA positive with additional MET markers [16–18,37,59,60].

Mechanistically, Le Loarer et al. found *SMARCB1* homozygous deletions by FISH in ~75% [16]. One case analyzed by WGS showed homozygous deletion and a complex chromoplexy event causing biallelic *NF1* loss and *SMARCB1* loss, with additional deletion of the second *SMARCB1* copy [37]. In contrast, an MSK-IMPACT/FISH analysis by one of us (JKD) found nonsense mutations without copy-number loss in 83%, with homozygous deletion in 1/6 (17%) [61]. Some studies reported *SMARCB1* loss in tumors with *EWSR1* rearrangement by FISH [16,59], which may have been caused by known false-positive *EWSR1* break-apart signals in cases with 22q11–12 regional alterations, which

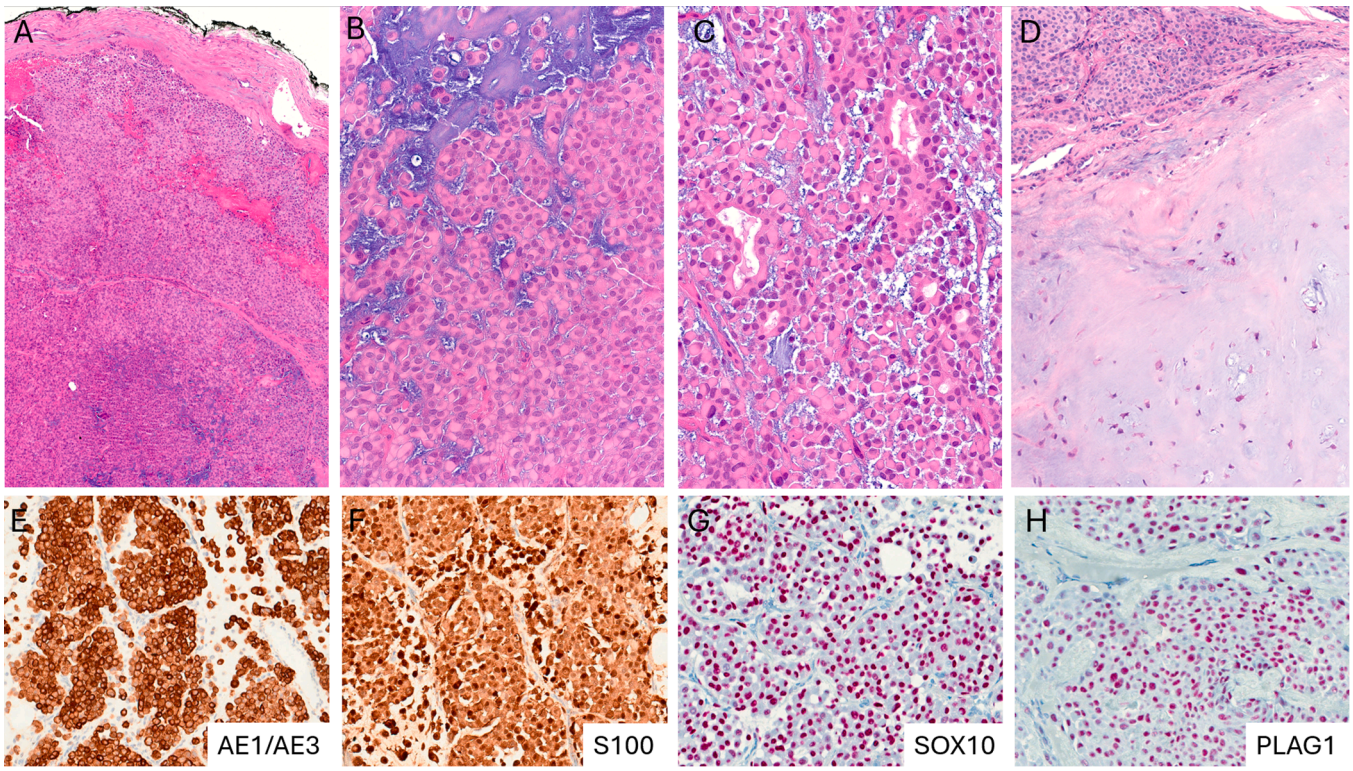

Fig. 8. *PLAG1*-rearranged cutaneous tumors. These neoplasms typically present as well-circumscribed dermal or subcutaneous nodules composed of epithelioid to plasmacytoid cells embedded in a myxoid stroma (**A, B**), with occasional ductal differentiation (**C**) and/or foci of hyaline cartilage (**D**). In contrast to FET-rearranged myoepithelial tumors, these adnexal neoplasms show consistent, diffuse, and strong immunoreactivity for AE1/AE3 (**E**), S100 protein (**F**), and SOX10 (**G**). Strong, diffuse nuclear expression of PLAG1 serves as a useful supportive diagnostic marker in the appropriate clinicopathologic context (**H**).

lead to SMARCB1-deletion [62]. However, *SMARCB1* loss has also been reported in an NGS-confirmed *EWSR1::POU5F1* MET [18], raising the possibility that SMARCB1 loss can occasionally occur as a secondary event in fusion-positive MET, further confounding interpretation and assembly of reliable data for genuine SMARCB1-loss driven MET.

MET with unknown molecular drivers

As this category includes only MET with comprehensive molecular testing yielding negative results, the available data are inherently sparse. Malik et al. reported three tumors consistent with MET on histology and methylation profiling (clustered with fusion confirmed MET on hierarchical and dimensionality reduction analyses), but lacking detectable fusions. Patients included two females and one male (ages 8, 33, 49), with tumors on trunk (n = 2) and face (n = 1). All were histologically malignant with high mitotic activity, and necrosis and composed of epithelioid/rhabdoid cells set in fibromyxoid stroma; one contained hyaline cartilage. All expressed S100, SOX10, and CK; 2/3 expressed EMA and GFAP. RNA-seq was fusion-negative; there was no chromosome 22 loss and no clustering with SMARCB1-deficient MET. Copy-number changes were non-recurrent (gain of chromosome 19 in one case; gain of 8q, 13, and 14 in another). Follow-up (n = 2) included NED at 12 months and DOD at 7 months [17].

When are morphology and IHC sufficient, and when is molecular testing needed?

The appropriate work-up of MET depends on access to molecular diagnostics. Morphology and IHC remain sufficient to diagnose MET, but often cannot assign a tumor to a molecular subgroup, thereby limiting prognostic stratification and increasing the risk of misclassification given the numerous MET mimics. Therefore, when feasible, molecular testing is desirable in most cases. That said, some subtypes are sufficiently distinctive that typical cases can be classified phenotypically (i.e. based on morphology and IHC), particularly the two predominantly cutaneous groups: *PLAG1*-rearranged cutaneous myoepitheliomas and syncytial myoepitheliomas with *EWSR1::PBX1/PBX3*. Particularly, a cutaneous location strongly favors a tumor falling under one of these two groups, which are themselves readily separable by morphology and IHC.

Regarding immunohistochemical markers of greatest diagnostic utility, we recommend a basic MET panel comprising S100 protein, SOX10, EMA, and broad-spectrum cytokeratins - preferably AE1/AE3 - with additional markers, including PLAG1, SMARCB1 or others selected according to the clinicopathologic context. Other so-called "myoepithelial markers" commonly employed in routine practice, such as GFAP, p63, or smooth muscle markers, lack sufficient sensitivity, specificity, or both to provide meaningful diagnostic support. For example, despite the limited number of molecularly tested cases stained for p63 (n = 11), only a single FET-rearranged MET in our analysis was positive. Therefore, the p63 expression reported in earlier MET series - already observed in only 23% of all MET cases [3]) - most likely reflects enrichment within the PLAG1-rearranged subgroup, in which p63 positivity has been documented in up to 59% of cases across multiple studies [20].

Terminology

WHO currently groups *PLAG1*-rearranged cutaneous (mixed) tumors and *FET*-rearranged deep soft tissue/bone tumors under the same MET umbrella. Given their distinct biology, we advocate for a clearer nosologic separation. *PLAG1*-altered lesions—true salivary gland analogs with anatomic proximity to normal cutaneous myoepithelial cells—should remain classified separately as cutaneous apocrine mixed tumors/myoepitheliomas.

In contrast, FET-rearranged tumors typically do not arise from anatomic locations containing native non-neoplastic myoepithelial cells,

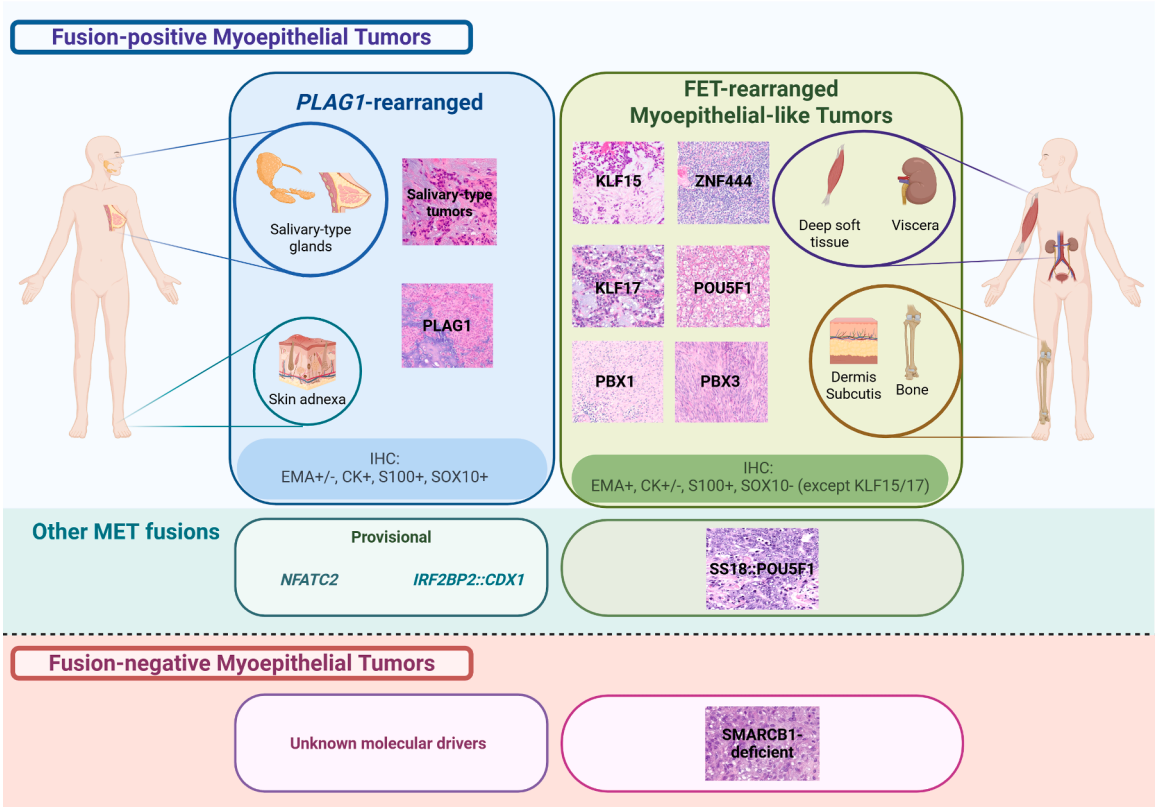

Fig. 9. Schematic of the proposed molecularly informed classification of MET with key diagnostic features.

nor display evidence of ductal/epithelial differentiation. More importantly, the WHO term "myoepithelial carcinoma", sometimes designated for malignant cases, is potentially misleading and can create clinical confusion, as these are not true carcinomas but behave as fusion-associated sarcomas, with parallels to entities such as ossifying fibromyxoid tumor, extraskeletal myxoid chondrosarcoma, and *NFATC2*-rearranged sarcoma. Malignant FET-rearranged tumors are thus better regarded as sarcomas rather than carcinomas [20]. Given how myoepithelial differentiation is poorly defined and the presence of clear subtype-specific differences in clinical behavior, we favor objective, fusion-defined terminology, e.g., benign/malignant *EWSR1::POU5F1*-rearranged myoepithelial-like tumor; benign/malignant SMARCB1-deficient myoepithelial-like tumor (Fig. 9), with grading determined mainly by histology.

Conclusion and future directions

While morphology and immunohistochemistry remain indispensable in the diagnostic work-up of MET, the incorporation of molecular testing and molecularly informed classification substantially improve diagnostic accuracy and refine prognostic stratification. From the foundational work of Dr. Fletcher and colleagues that laid the initial conceptual and diagnostic framework for MET through the molecular advances driven particularly by Dr Antonescu and colleagues, to the most recent epigenetic studies, the past three decades have clarified that MET comprise a rare but highly heterogeneous family of tumors.

Major gaps remain, however, particularly for fusion-negative tumors, underscoring the need for larger clinicopathologic and comprehensive genomic studies. Most importantly, optimal therapy remains undefined. As in other areas of oncologic pathology, progress in treatment will depend on precise classification and improved understanding of pathogenesis. We hope that the refined nomenclature and molecular framework proposed here represent practical steps toward that goal.

Declaration of interest statement

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CRediT authorship contribution statement

Michael Michal: Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Supervision, Writing – original draft. **Josephine K Dermawan:** Conceptualization, Data curation, Formal analysis, Visualization, Writing – review & editing.

Declaration of competing interest

The authors have no relevant financial or non-financial interests to disclose.

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References

1. Kilpatrick SE, Hitchcock MG, Kraus MD, et al. Mixed tumors and myoepitheliomas of soft tissue: a clinicopathologic study of 19 cases with a unifying concept. *Am J Surg Pathol.* 1997;21:13–22.
2. Jo VY, Hornick JL, Antonescu CR, et al. *WHO Classification of Tumours. Soft tissue and Bone Tumours*. Lyon, France: International Agency for Research on Cancer; 2020.
3. Hornick JL, Fletcher CD. Myoepithelial tumors of soft tissue: a clinicopathologic and immunohistochemical study of 101 cases with evaluation of prognostic parameters. *Am J Surg Pathol.* 2003;27:1183–1196.
4. Antonescu CR, Zhang L, Chang NE, et al. EWSR1-POU5F1 fusion in soft tissue myoepithelial tumors. a molecular analysis of sixty-six cases, including soft tissue, bone, and visceral lesions, showing common involvement of the EWSR1 gene. *Genes Chromosomes Cancer.* 2010;49:1114–1124.
5. Huang SC, Chen HW, Zhang L, et al. Novel FUS-KLF17 and EWSR1-KLF17 fusions in myoepithelial tumors. *Genes Chromosomes Cancer.* 2015;54:267–275.
6. Agaram NP, Chen HW, Zhang L, et al. EWSR1-PBX3: a novel gene fusion in myoepithelial tumors. *Genes Chromosomes Cancer.* 2015;54:63–71.
7. Cajaiba MM, Jennings LJ, Rohan SM, et al. Expanding the spectrum of renal tumors in children: primary renal myoepithelial carcinomas with a novel EWSR1-KLF15 Fusion. *Am J Surg Pathol.* 2016;40:386–394.
8. Suurmeijer AJH, Dickson BC, Swanson D, et al. A morphologic and molecular reappraisal of myoepithelial tumors of soft tissue, bone, and viscera with EWSR1 and FUS gene rearrangements. *Genes Chromosomes Cancer.* 2020;59:348–356.
9. Antonescu CR, Agaram NP, Sung YS, et al. Undifferentiated round cell sarcomas with novel SS18-POU5F1 fusions. *Genes Chromosomes Cancer.* 2020;59:620–626.
10. Argani P, Matoso A, Gross JM, et al. Primary renal sarcoma with SS18::POU5F1 gene fusion. *Genes Chromosomes Cancer.* 2022;61:572–577.
11. Shenoy A, Newsom K, Gray B, et al. Malignant round cell tumor with SS18-POU5F1 fusion: is it a myoepithelial neoplasm, a synovial sarcoma or a new entity? *Histopathology.* 2020;77:681–684.
12. Liu Z, Yuan H, Han M. Therapeutic response of soft tissue sarcoma with novel SS18-POU5F1 fusion: a case report. *Front Oncol.* 2021;11, 666946.
13. Antonescu CR, Zhang L, Shao SY, et al. Frequent PLAG1 gene rearrangements in skin and soft tissue myoepithelioma with ductal differentiation. *Genes Chromosomes Cancer.* 2013;52:675–682.
14. Bahrami A, Dalton JD, Krane JF, et al. A subset of cutaneous and soft tissue mixed tumors are genetically linked to their salivary gland counterpart. *Genes Chromosomes Cancer.* 2012;51:140–148.
15. Mansour B, Donati M, Pancsa T, et al. Molecular analysis of apocrine mixed tumors and cutaneous myoepitheliomas: a comparative study confirming a continuous spectrum of one entity with near-ubiquitous PLAG1 and rare mutually exclusive HMGA2 gene rearrangements. *Virchows Arch.* 2025;486:215–223.
16. Le Loarer F, Zhang L, Fletcher CD, et al. Consistent SMARCB1 homozygous deletions in epithelioid sarcoma and in a subset of myoepithelial carcinomas can be reliably detected by FISH in archival material. *Genes Chromosomes Cancer.* 2014;53:475–486.
17. Malik F, Koo SC, Din NU, et al. Reappraisal of soft tissue myoepithelial tumors by DNA methylation profiling reveals an epigenetically distinct group of mostly fusion-driven neoplasms. *Virchows Arch.* 2025;486:573–584.
18. Logan SJ, Dehner CA, Alruwaii FI, et al. Myoepithelial tumors of soft tissue and bone in children and young adults: a clinicopathologic study of 40 cases occurring in patients </= 21 Years of age. *Hum Pathol.* 2024;149:10–20.
19. Jurmeister P, Leitheiser M, Arnold A, et al. DNA methylation profiling of salivary gland tumors supports and expands conventional classification. *Mod Pathol.* 2024;37, 100625.
20. Michal M, Malik F, Mansour B, et al. FET-rearranged myoepithelial tumors are clinically heterogeneous and epigenetically distinct from PLAG1-rearranged adnexal and salivary gland myoepithelial tumors. *Clin Cancer Res.*. 2025.
21. Macagno N, Kervarrec T, Thanguturi S, et al. SOX10-internal tandem duplications and PLAG1 or HMGA2 fusions segregate eccrine-type and apocrine-type cutaneous mixed tumors. *Mod Pathol.* 2024;37, 100430.
22. Martins C, Fonseca I, Roque L, et al. PLAG1 gene alterations in salivary gland pleomorphic adenoma and carcinoma ex-pleomorphic adenoma: a combined study using chromosome banding, in situ hybridization and immunocytochemistry. *Mod Pathol.* 2005;18:1048–1055.
23. Alsugair Z, Donzel M, Macagno N, et al. Exploring the molecular landscape of cutaneous mixed tumors characterized by TRPS1::PLAG1 gene fusion. *J Pathol.* 2024;264:448–456.
24. Nacev BA, Jones KB, Intlekofer AM, et al. The epigenomics of sarcoma. *Nat Rev Cancer.* 2020;20:608–623.
25. Michal M, Rubin BP, Agaimy A, et al. EWSR1-PATZ1-rearranged sarcoma: a report of nine cases of spindle and round cell neoplasms with predilection for thoracoabdominal soft tissues and frequent expression of neural and skeletal muscle markers. *Mod Pathol.* 2021;34:770–785.
26. Dehner CA, Torres-Mora J, Gupta S, et al. Sarcomas harboring EWSR1::PATZ1 fusions: a clinicopathologic study of 17 Cases. *Mod Pathol.* 2024;37, 100400.
27. Klubickova N, Dermawan JK, Mosaieby E, et al. Comprehensive clinicopathological, molecular, and methylation analysis of mesenchymal tumors with NTRK and other kinase gene aberrations. *J Pathol.* 2024;263:61–73.
28. Suurmeijer AJH, Dickson BC, Swanson D, et al. A novel group of spindle cell tumors defined by S100 and CD34 co-expression shows recurrent fusions involving RAF1, BRAF, and NTRK1/2 genes. *Genes Chromosomes Cancer.* 2018;57:611–621.
29. Gelarden IA, Fu L, Yap KL, et al. Cytology-histology correlation of myoepithelial tumors harboring EWSR1-POU5F1 fusions: a report of two cases. *Diagn Cytopathol.* 2022;50:E163–E169.
30. Deng FM, Galvan K, de la Roza G, et al. Molecular characterization of an EWSR1-POU5F1 fusion associated with a t(6;22) in an undifferentiated soft tissue sarcoma. *Cancer Genet.* 2011;204:423–429.
31. Yamaguchi S, Yamazaki Y, Ishikawa Y, et al. EWSR1 is fused to POU5F1 in a bone tumor with translocation t(6;22)(p21;q12). *Genes Chromosomes Cancer.* 2005;43:217–222.
32. Dabska M. Parachordoma: a new clinicopathologic entity. *Cancer.* 1977;40:1586–1592.
33. Pizem J, Bostjancic E, Sekoranja D, et al. Pigmented (melanotic) myoepithelial tumor of soft tissue with EWSR1-KLF17 fusion. *Cancer Genet.* 2020;246-247:48–52.
34. Bodis S, Kroiss S, Tchinda J, et al. Myoepithelial Carcinoma of soft tissue With an EWSR1-KLF15 gene fusion in an infant. *Pediatr Dev Pathol.* 2021;24:371–377.
35. Stevens TM, Qarmali M, Morlote D, et al. Malignant ewing-like neoplasm With an EWSR1-KLF15 Fusion: at the crossroads of a myoepithelial carcinoma and a ewing-like sarcoma. a case report with treatment options. *Int J Surg Pathol.* 2018;26:440–447.
36. Patel P, Roberts R, Cole J, et al. A rare case of an intracardiac myoepithelial carcinoma in an infant. *J Pediatr Hematol Oncol.* 2019;41:e206–e209.
37. Cyrta J, Rosiene J, Bareja R, et al. Whole-genome characterization of myoepithelial carcinomas of the soft tissue. *Cold Spring Harb Mol Case Stud.* 2022;8.
38. Brandal P, Panagopoulos I, Bjerkehagen B, et al. t(19;22)(q13;q12) Translocation leading to the novel fusion gene EWSR1-ZNF444 in soft tissue myoepithelial carcinoma. *Genes Chromosomes Cancer.* 2009;48:1051–1056.
39. Jo VY, Antonescu CR, Zhang L, et al. Cutaneous syncytial myoepithelioma: clinicopathologic characterization in a series of 38 cases. *Am J Surg Pathol.* 2013;37:710–718.
40. Wangsiricharoen S, Gjeorgjievski SG, Bahrami A, et al. Non-cutaneous syncytial myoepitheliomas are identical to cutaneous counterparts: a clinicopathologic study of 24 tumors occurring at diverse locations. *Virchows Arch.* 2023;483:665–675.
41. Mehta A, Davey J, Gharpuray-Pandit D, et al. Cutaneous myoepithelial neoplasms on acral sites show distinctive and reproducible histopathologic and immunohistochemical features. *Am J Surg Pathol.* 2022;46:1241–1249.
42. Jo VY, Antonescu CR, Dickson BC, et al. Cutaneous syncytial myoepithelioma is characterized by recurrent EWSR1-PBX3 fusions. *Am J Surg Pathol.* 2019;43:1349–1354.
43. Dehner CA, Johnson EF, Wieland CN, et al. Fusion-driven cutaneous and superficial mesenchymal and adnexal tumors-a clinicopathologic and molecular study of 15 cases, including a novel case of ACTB::ZMIZ2-rearranged adnexal carcinoma. *J Cutan Pathol.* 2024;51:538–548.
44. Haglund C, Zemmler M, Tsagkozis P, et al. An intraosseous myoepithelial carcinoma with a EWSR1::PBX3 fusion. *Genes Chromosomes Cancer.* 2023;62:607–610.
45. Yun S, Kim SH, Cho HS, et al. EWSR1-PBX3 fused myoepithelioma arising in metatarsal bone: case report and review of the literature. *Pathol Int.* 2019;69:42–47.
46. Gandhi JS, Schneider T, Thangaiah JJ, et al. Myoepithelial tumors of bone With EWSR1::PBX3 fusion: a spectrum from benign to malignant. *Mod Pathol.* 2024;37, 100514.
47. Oon ML, Wu B, Lee JJL, et al. SS18::POU5F1-fused sarcoma of the parotid with divergent ganglioneuromatous differentiation-a novel manifestation of a rare tumor. *Virchows Arch.* 2025.
48. Kazakov DV, Belousova IE, Bisceglia M, et al. Apocrine mixed tumor of the skin ("mixed tumor of the folliculosebaceous-apocrine complex"). Spectrum of differentiations and metaplastic changes in the epithelial, myoepithelial, and stromal components based on a histopathologic study of 244 cases. *J Am Acad Dermatol.* 2007;57:467–483.
49. Ferreiro JA, Nascimento AG. Hyaline-cell rich chondroid syringoma. A tumor mimicking malignancy. *Am J Surg Pathol.* 1995;19:912–917.
50. Le Loarer F, Szuhai K, Tirode F. *WHO Classification of Tumours. Soft tissue and Bone Tumours*. Lyon, France: International Agency for Research on Cancer; 2020.
51. Wang GY, Thomas DG, Davis JL, et al. EWSR1-NFATC2 translocation-associated sarcoma clinicopathologic findings in a rare aggressive primary bone or soft tissue tumor. *Am J Surg Pathol.* 2019;43:1112–1122.
52. Hornick JL, Dal Cin P, Fletcher CD. Loss of INI1 expression is characteristic of both conventional and proximal-type epithelioid sarcoma. *Am J Surg Pathol.* 2009;33:542–550.
53. Gleason BC, Fletcher CD. Myoepithelial carcinoma of soft tissue in children: an aggressive neoplasm analyzed in a series of 29 cases. *Am J Surg Pathol.* 2007;31:1813–1824.
54. Kinoshita I, Kohashi K, Yamamoto H, et al. Myxoepithelioid tumour with chordoid features: a clinicopathological, immunohistochemical and genetic study of 14 cases of SMARCB1/INI1-deficient soft-tissue neoplasm. *Histopathology.* 2021;79:629–641.
55. Folpe AL, Schoolmeester JK, McCluggage WG, et al. SMARCB1-deficient vulvar neoplasms: a clinicopathologic, immunohistochemical, and molecular genetic study of 14 cases. *Am J Surg Pathol.* 2015;39:836–849.
56. Yoshida A, Yoshida H, Yoshida M, et al. Myoepithelioma-like tumors of the vulvar region: a distinctive group of SMARCB1-deficient Neoplasms. *Am J Surg Pathol.* 2015;39:1102–1113.
57. Han W, Zhu X, Li X, et al. SMARCB1 (INI-1)-deficient myoepithelioma-like tumor in the perineal region of a male patient: a case report. *Int J Surg Pathol.* 2025, 10668969251382738.
58. Yin X, Yang X, Wang S, et al. SMARCB1/INI1-deficient epithelioid and myxoid neoplasms in paratesticular region: expanding the clinicopathologic and molecular spectrum. *Ann Diagn Pathol.* 2024;68, 152242.

59. Rekhi B, Sable M, Jambhekar NA. Histopathological, immunohistochemical and molecular spectrum of myoepithelial tumours of soft tissues. *Virchows Arch.* 2012; 461:687–697.
60. Agaimy A, Naroditsky I, Ben-Izhak O. Primary high-grade myoepithelial carcinoma of the lung: a study of three cases illustrating frequent SMARCB1-deficiency and review of the literature. *Ann Diagn Pathol.* 2021;53, 151759.
61. Dermawan JK, Singer S, Tap WD, et al. The genetic landscape of SMARCB1 alterations in SMARCB1-deficient spectrum of mesenchymal neoplasms. *Mod Pathol.* 2022;35:1900–1909.
62. Huang SC, Zhang L, Sung YS, et al. Secondary EWSR1 gene abnormalities in SMARCB1-deficient tumors with 22q11-12 regional deletions: potential pitfalls in interpreting EWSR1 FISH results. *Genes Chromosomes Cancer*. 2016;55:767–776.