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The pericyte antigen RGS5 in perivascular soft tissue tumors☆,,☆☆

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Summary

Perivascular soft tissue tumors are relatively uncommon neoplasms of unclear lineage of differentiation, although most are presumed to originate from or differentiate to pericytes or a modified perivascular cell. Among these, glomus tumor, myopericytoma, and angioleiomyoma share a spectrum of histologic findings and a perivascular growth pattern. In contrast, solitary fibrous tumor was once hypothesized to have pericytic differentiation—although little bona fide evidence of pericytic differentiation exists. Likewise the perivascular epithelioid cell tumor (PEComa) family shares a perivascular growth pattern, but with distinctive dual myoid-melanocytic differentiation. RGS5, regulator of G-protein signaling 5, is a novel pericyte antigen with increasing use in animal models. Here, we describe the immunohistochemical expression patterns of RGS5 across perivascular soft tissue tumors, including glomus tumor (n = 6), malignant glomus tumor (n = 4), myopericytoma (n = 3), angioleiomyoma (n = 9), myofibroma (n = 4), solitary fibrous tumor (n = 10), and PEComa (n = 19). Immunohistochemical staining and semi-quantification was performed, and compared to αSMA (smooth muscle actin) expression. Results showed that glomus tumor (including malignant glomus tumor), myopericytoma, and angioleiomyoma shared a similar diffuse immunoreactivity for RGS5 and αSMA across all tumors examined. In contrast, myofibroma, solitary fibrous tumor and PEComa showed predominantly focal to absent RGS5 immunoreactivity. These findings further support a common pericytic lineage of differentiation in glomus tumors, myopericytoma and angioleiomyoma. The pericyte

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marker RGS5 may be of future clinical utility for the evaluation of pericytic differentiation in soft tissue tumors.

Keywords

RGS5; Glomus tumor; Myopericytoma; Angioleiomyoma; Solitary fibrous tumor; Hemangiopericytoma; Pericyte

1. Introduction

Perivascular soft tissue tumors are relatively uncommon neoplasms of unclear lineage of differentiation. Among these, glomus tumor, myopericytoma, and angioleiomyoma share a spectrum of histologic findings, including a perivascular growth pattern. Glomus tumor is a subcutaneous and soft tissue neoplasm [1], with recently discovered recurrent *MIR143-NOTCH* fusion gene [2]. Myopericytoma is composed of eosinophilic tumor cells with more distinct smooth muscle differentiation and a whorled perivascular pattern. Angioleiomyoma is commonly a painful subcutaneous nodule, with a histological appearance of more differentiated smooth muscle. Notably, there is well-recognized overlap between these tumors [3]. Moreover, immunohistochemical staining patterns across these tumors are relatively similar, and include immunoreactivity to α smooth muscle actin (αSMA), muscle-specific actin (MSA), and h-caldesmon. Other soft tissue tumors have been previously hypothesized to have pericytic differentiation. For example, solitary fibrous tumor, previously termed *hemangiopericytoma*, was once thought to demonstrate pericytic differentiation based on ultrastructural descriptions [4]. The perivascular epithelioid cell tumor (PEComa) family of tumors shares a perivascular growth pattern but has well-described and distinctive dual myoidmelanocytic differentiation [1,5].

Pericytes are mesenchymal cells that closely enwrap small blood vessels, regulating and supporting the microvasculature through direct contact with the endothelium. Pericytes demonstrate a distinct immunohistochemical profile, including expression of αSMA, CD146, and PDGFRβ, without endothelial differentiation (absence of CD31, CD34 immuno-reactivity) [6]. Ultrastructural examination has suggested either a modified pericyte or smooth muscle phenotype in glomus tumor [7,8], myopericytoma, and angioleiomyoma [9]. Recently, we reported a shared pericyte immunophenotype among glomus tumor, myopericytoma, and angioleiomyoma, including diffuse immunoreactivity for αSMA, CD146, and PDGFRβ [10]. However, these known pericyte antigens have relatively diverse expression profiles, both in normal and neoplastic tissues (see Shih et al and Palman et al [11,12] for a review). Here, we examine the novel pericyte marker RGS5 in these perivascular soft tissue tumors.

RGS5, regulator of G-protein signaling 5, is a novel and potentially specific pericyte marker. Since the identification of human RGS5 [13], investigators identified RGS5 as robustly expressed in pericytes [14–16]. Bondjers et al confirmed RGS5 as a pericyte marker, showing that pericyte-deficient mice (PDGFβ and PDGFRβ null mice) lack RGS5 expression [15]. RGS5 appears to be a marker rather than a requirement for pericyte differentiation, as RGS5-deficient mice apparently show normal pericyte coverage of

vasculature [17]. Berger et al and others have found that pericyte-derived RGS5 expression is elevated in diverse contexts of increased angiogenesis, including wound healing and tumor angiogenesis [18,19]. Conversely, multiple investigators have found that atherosclerotic changes are associated with loss of RGS5 expression [20]. Despite accumulating evidence to suggest the utility of RGS5 as a marker of pericytic differentiation in animal studies, to date the expression patterns of RGS5 in perivascular soft tissue tumors are entirely unknown.

2. Materials and methods

2.1. Histology and immunohistochemistry

Tumors were identified using a retrospective chart review of the pathology tissue archives of the Department of Pathology and Laboratory Medicine at the University of California, Los Angeles (UCLA) using the search terms “glomus tumor, myopericytoma, angioleiomyoma, myofibroma, solitary fibrous tumor, angiomyolipoma, and PEComa”. Slides were reviewed by two independent pathologists to ensure accuracy of diagnosis (S.M.D and A.W.J). Diagnostic criteria for malignancy in glomus tumor were used as described by Folpe and colleagues [1,21], including deep-seated tumors greater than 2 cm, tumors with atypical mitotic figures, or tumors with moderate to high nuclear grade and >5 mitotic figures in 50 HPF. Recognizing that agreement does currently not exist regarding criteria for malignancy in angiomyolipoma (AML), we chose the criteria set forth by Brimo et al to distinguish malignant potential in renal angiomyolipoma [22]. Briefly, a designation of malignant AML was given when 3 of the following four criteria were present: (1) ≥70% atypical epithelioid cells, (2) ≥2 mitoses per 10 HPF, (3) presence of atypical mitotic figures, and (4) presence of necrosis. Patient information was obtained, including age, sex, tumor location, tumor size, and previous immunohistochemical stains performed during the initial diagnostic evaluation. Formalin-fixed, paraffin-embedded tumor tissue from patients were acquired from the tissue archives, under UCLA IRB approval #13–000918.

Immunohistochemistry for pericyte markers was performed using the ABC method (Vectastain Elite ABC; Vector Laboratories, Burlingame, CA) using diaminobenzidine (DAB) as the chromogen (ImmPACT DAB, Vector Laboratories). Multiple antigens were detected by multiplexing the ABC method, and DAB chromogen, with an alkaline phosphatase polymer detection method (ImmPress-AP Polymer Detection, Anti-mouse IG, Vector Laboratories). The following primary antibodies were used: monoclonal mouse anti-αSMA (1:75, [1A4], ABCAM), and monoclonal mouse anti-RGS5 (1:100, [89C2], Cell Signaling Technologies). The following secondary antibodies were used: polyclonal goat biotinylated anti-rabbit IgG (1:500, Sigma, St Louis, MO), polyclonal horse anti-mouse IgG (1:500, [H + L], Vector Laboratories), polyclonal goat anti-rat Ig (1:500, Becton Dickinson and Company).

Heat-mediated antigen retrieval was performed for all immunohistochemical stains in 1 mmol/L tris-EDTA, 0.01% Tween-20 (Sigma), pH 8. Nonspecific antibody binding was blocked (IHC-TEK Antibody Diluent, pH 7.4; IHC World, LLC, Woodstock, MD). Endogenous peroxidase and alkaline phosphatase blocking solution was used (BLOXALL endogenous peroxidase and alkaline phosphatase blocking solution, Vector Laboratories). Mayer's hematoxylin was used as a nuclear counterstain (1:5, ABCAM), and slides were

mounted using aqueous media (VectaMount AQ, Vector Laboratories). In all cases, immunohistochemical staining without primary antibody was used as a negative control.

2.2. Immunohistochemical semi-quantitation

Semi-quantitative grading of immunohistochemical stains was performed with some modification of previous protocols by three blinded independent observers [10]. Intensity of staining was graded on a three point scale (0–3+), defined as follows: 0: absent stain; 1+: weak, focal cytoplasmic staining; 2+: moderate, focal to diffuse cytoplasmic staining; 3+: strong, diffuse cytoplasmic staining. In cases of disagreement between observers, tumor staining was re-evaluated by the same observers and the majority opinion was selected. In addition, the percentage of tumor cells stained was also evaluated, using a 5% incremental scale, and averages between observers were calculated. Statistical analysis of semi-quantitation was performed when appropriate, using a 2-sample Wilcoxon rank-sum (Mann-Whitney *U*) test, using STATA. $P < .05$ was considered significant.

3. Results

3.1. RGS5 expression in glomus tumor

RGS5 expression was examined in six glomus tumors specimens. Glomus tumors were all located on fingers and ranged in size from 0.4 to 0.8 cm. Tumors examined showed either solid or glomuvenous growth patterns (Fig. 1). Clinical immunohistochemical stains included diffuse immunoreactivity for αSMA and MSA. All tumors were negative for epithelial markers and melanocytic markers when examined. Significant cytoplasmic immunoreactivity for RGS5 in glomus tumor cells was noted in the majority of tumor cells, observed both in solid growth patterns (Fig. 1C–E) and those glomus tumors with a glomuvenous growth pattern (not shown). Next, semi-quantitation of immunohistochemical staining was performed (Tables 1 and 2). Moderate immunoreactivity for RGS5 was observed in the majority of tumors (2+ staining intensity or greater in 5/6 samples). RGS5 immunoreactivity was widely distributed across all tumor cells (>65% of tumor cells in 5/6 samples).

Next, RGS5 expression was evaluated across four malignant glomus tumor specimens. In our study, all tumors were deep-seated and ranged in size from 4.5 to 5.5 cm. Increased mitotic rate was seen in three of four tumors (9–25 mitoses per 10 HPF). Moderate to high nuclear grade was seen in one case. Clinical immunohistochemical stains included immunoreactivity for αSMA, and no expression of epithelial markers, melanocytic markers or endothelial markers when performed. No recurrence or metastasis was documented in any case, with a mean follow-up period of 8.25 months. Next, RGS5 expression was interrogated in each malignant glomus specimen by immunohistochemistry (Fig. 2). Results showed that all tumors showed diffuse RGS5 immunoreactivity, similar to their benign glomus tumor counterparts. Adjacent, non-lesional blood vessels served as an internal positive control for RGS5 immunoreactivity (black arrowheads). Next, semi-quantification of immunohistochemical stains was performed (Tables 1 and 2). At least moderate immunoreactivity for RGS5 was seen in the majority of cases (2+ intensity or greater in 4/4 tumor samples). Likewise, all tumors demonstrated greater than 50% immunoreactivity

among tumor cells (4/4 samples). In summary, RGS5 expression was reliably observed across all benign and malignant glomus tumor specimens. No significant difference in RGS5 expression was seen between benign and malignant glomus tumors ($P = .86$ and .50 for intensity and distribution of staining, respectively).

3.2. RGS5 expression in myopericytoma

Next, RGS5 expression was examined in three myopericytoma specimens. All tumors were of the superficial soft tissues, located in the distal lower extremity, and ranged in size from 0.9 to 3.0 cm. Clinical immunohistochemical stains showed positivity for αSMA, and negativity for epithelial and melanocytic markers when performed. RGS5 expression was next examined in each myopericytoma sample (Fig. 3). Similar to glomus tumor specimens, diffuse and cytoplasmic immunoreactivity for RGS5 was observed. Next, semi-quantitation was performed (Tables 1 and 2). Moderate RGS5 immunoreactivity was seen in all cases (2+, 3/3 cases) and found diffusely across tumor cells (>90% distribution in all cases).

3.3. RGS5 expression in angioleiomyoma

RGS5 expression was next examined in nine angioleiomyoma specimens. All tumors were found in the dermis and superficial soft tissues of the distal upper and lower extremities, ranging in size from 0.7 to 2.5 cm. Tumors typically showed characteristics of both venous and fascicular growth patterns (Fig. 4). Clinical immunohistochemical stains demonstrated positivity for αSMA, MSA and desmin, when examined. All angioleiomyoma specimens showed negative immunohistochemical staining for vascular markers when performed. Next, the intensity and distribution of RGS5 expression was examined (Fig. 4). Interestingly, RGS5 expression differed substantially based on the growth pattern within the tumor. Areas of venous-type growth pattern with a prominent perivascular arrangement of tumor cells showed stronger and more defined immunoreactivity for RGS5 (Fig. 4D–F). In contrast, areas of more prominent fascicular or sheet-like growth showed predominant αSMA immunoreactivity only, with less RGS5 expression (Fig. 4G–I). These immunohistochemical results were next quantified both in terms of intensity and distribution of stain (Tables 1 and 2). The vast majority of tumors demonstrated RGS5 immunoreactivity (1+–3+ intensity, 8/9 tumor samples). As well, diffuse RGS5 immunoreactivity was noted in the majority of angioleiomyoma samples (≥80% staining distribution in 8/8 cases).

3.4. RGS5 expression in myofibroma

RGS5 expression was next examined in four myofibroma specimens. All tumors were reported as solitary rather than multicentric and were found in a wide array of anatomic locations. Most tumors showed a characteristic zonal appearance with myoid nodules with intervening cellular areas (Fig. 5). Clinical immunohistochemical stains demonstrated positivity for αSMA and MSA, when examined. All specimens showed negative immunohistochemical staining for epithelial markers, desmin and S100, when performed. Next, the intensity and distribution of RGS5 expression was examined (Fig. 5). Interestingly and in contrast to previously examined tumor types, RGS5 expression was predominantly limited to intratumoral blood vessels. These immunohistochemical results were next quantified both in terms of intensity and distribution of stain (Tables 1 and 2). Only a

minority of tumors demonstrated RGS5 immunoreactivity (2+ intensity, 5% distribution in 1/4 tumor samples).

3.5. RGS5 expression in solitary fibrous tumor

Solitary fibrous tumors (SFTs) were examined in ten patient samples. Tumors were most commonly in the deep soft tissues. Within the tumors examined, a range of appearances were seen from more “solitary fibrous tumor”-like (Fig. 6A) to more hemangiopericytoma-like in appearance (Fig. 6B). Two diagnoses of “atypical SFT+ were included, both of which showed increased mitotic activity (4–8 mitoses per 10 HPF) but without other features of malignancy (no increased cellularity, no cytologic atypia, and no necrosis). No recurrence or metastases was documented in either case of “atypical SFT” (mean follow-up period: 2.5 months). Clinical immunohistochemical stains included positivity for CD34, as well as BCL2 and CD99 when examined. In all cases, epithelial markers, melanocytic markers, and vascular markers were negative. Results showed that in many areas immunoreactivity for RGS5 was essentially confined to the intralesional blood vessels (Fig. 6C–E). High magnification revealed flattened αSMA+ RGS5+ cells along the abluminal surface of blood vessels, morphologically consistent with pericytes (Fig. 6E). In many cases weak to moderate immunoreactivity for RSG5 was observed in tumor cells (1+-2+), predominantly in a focal distribution (<50% distribution in 8/8 samples) (Fig. 6F and G).

In summary, RGS5 expression was found in a weak and focal distribution in most SFT samples, with stronger expression essentially limited to intralesional blood vessels. Moreover, the intensity and distribution of RGS5 immunoreactivity in SFT was significantly reduced in comparison to glomus tumor, myopericytoma and angioleiomyoma ($P \leq .05$ and $P \leq .03$ for staining intensity and distribution, respectively).

3.6. RGS5 expression in PEComa family tumors

The PEComa family was next examined (Fig. 7). Tumors were most commonly in a renal/perirenal location, but also included pelvic, retroperitoneal, and hepatic locations. A variety of histologic patterns were observed, including the typical triphasic appearance with myoid cells, thick-walled vasculature, and tumor cells resembling adipocytes (n = 5). In addition, tumors with predominantly spindled or epithelioid tumor cells were also examined, designated as spindled AML (n = 6) and epithelioid AML (n = 4), respectively. Unusual tumors included malignant PEComa (n = 1), as well as lymphangiomyoma (n = 3). All cases of lymphangiomyoma were incidental operative findings during a separate procedure. A history of tuberous sclerosis was not present in any case. Clinical immunohistochemical stains included positivity for melanocytic markers, including HMB45 (94.7%), MART1 (88.9%), and S100 (72.7%). When assessed, smooth muscle markers were also primarily positive, including SMA (81.8%) and desmin (75%). Epithelial markers were uniformly negative. RGS5 expression was examined across each PEComa sample (Tables 1 and 2). As with SFT, results showed that in many cases immunoreactivity for RGS5 was predominantly confined to the intralesional blood vessels (Fig. 7B–D), with complete absence of tumor cell staining in 42.1% of samples (8/19 cases). In some cases weak to moderate immunoreactivity for RSG5 was observed in tumor cells (1+-2+), predominantly in a focal distribution (<50% distribution in 11/11 samples) (Fig. 7E–G).

In summary, RGS5 expression was either absent or found in a weak and focal distribution in all PEComa samples. Moreover, the intensity and distribution of RGS5 immunoreactivity in PEComa was significantly reduced in comparison to glomus tumor, myopericytoma and angioleiomyoma ($P \leq .02$ and $P \leq .0001$ for staining intensity and distribution, respectively).

4. Discussion

In summary, the pericyte marker RGS5 demonstrates consistent expression across perivascular soft tissue tumors, including glomus tumor, myopericytoma and angioleiomyoma. These findings extend our previous observation regarding a shared pericytic immunophenotype within these tumors, including immunoreactivity for αSMA, CD146, and PDGFRβ [10]. In contrast, myofibroma, solitary fibrous tumor and PEComa tumors do not share this pericytic immunophenotype, with absent or weak/focal RSG5 immunoreactivity only. These findings give further support to the classification of glomus tumor, myopericytoma and angioleiomyoma as pericytic tumors.

Unfortunately, no known pericytic markers are absolutely specific. However, based on the available literature and the present study, RGS5 immunoreactivity in combination with αSMA+CD146+PDGFRβ+ is quite specific for pericytic differentiation. As expected, RSG5 expression is seen in other neoplasms. For example, RGS5 expression can be found in parathyroid adenoma [23], gastric [24], lung [25], and hepatocellular carcinomas [26], as well as multiple lymphomas [26]. Clearly RGS5 has other biologic functions beyond its role in pericyte identity and/or function. Other possible pericyte markers have yet to be investigated in perivascular soft tissue tumors, including Ang-1 and Ang-2 [27,28], and nestin [28].

Current interests in pericytes predominantly owe to the growing understanding that this cell type represents mesenchymal stem cell (MSC) progenitor cells [6,29–33]. In fact, the identity of pericytes as the native in vivo progenitors of MSC explains their ubiquitous presence throughout the body. Purified pericytes give rise to multiple mesodermal tissues after in vitro differentiation or in vivo transplantation, including bone, adipose, cartilage, and muscle—features identical to traditionally derived MSC [33,34]. While the isolation and utilization of pericytes is a topic of excitement to those in the fields of stem cell biology and tissue engineering, it is unclear what, if any, relationship this MSC identity has with perivascular soft tissue tumors. MSC markers have not yet been examined in situ among perivascular tumors. Of note, ectopic ossification, chondrogenesis or adipogenesis is not commonly encountered among perivascular soft tissue tumors. Therefore, the extent to which perivascular soft tissue tumors demonstrate MSC characteristics remains a question yet to be answered.

Solitary fibrous tumor, previously termed hemangiopericytoma, had been previously posited to have pericytic differentiation, based on cytomorphology and ultrastructural findings [4,35]. Recurrent cytogenetic abnormalities involving the *NAB-STAT6* gene fusion have been recently described among SFT samples in both pleural and extrapleural locations [36]. To date there is no direct evidence that SFT arises from pericytic cells (see [37] for a review). Previously, we examined αSMA, CD146 and PDGFRβ expression across 10 SFT

specimens [10]. No expression of αSMA or CD146 was seen, while patchy PDGFRβ immunoreactivity was found in a subset of SFT (7/10 samples), in line with previously published observations [38]. Here, we extend these findings with focal and weak RGS5 immunoreactivity in 8/10 SFT samples. As others have suggested, these features collectively argue against pericytic differentiation within SFT.

A somewhat unexpected finding in the present study was the limited expression of RGS5 expression in myofibroma specimens. It is well documented that the cellular elements of myofibroma/myofibromatosis have significant histologic overlap with myopericytoma, and in some cases definitive diagnosis is not feasible [3,39]. In fact, the umbrella term “perivascular myomas” has been previously proposed to cover these similarly appearing tumors, although this is not widely accepted terminology [3]. More study is required in order to better elucidate the cellular differences between RGS5+ tumors (glomus tumor, myopericytoma, angioleiomyoma) and RGS5–tumors (myofibroma). In our previous study, we found that a minority of soft tissue tumors demonstrate loss of PDGFRβ expression, potentially representing a modified or aberrant pericyte immunophenotype [10]. Lack of RGS5 in myofibroma may represent such aberrant pericyte phenotype, or alternatively could suggest a non-pericytomatous line of differentiation.

In summary, diffuse RGS5 expression in perivascular neoplasms lends further support to pericytic differentiation in glomus tumors, myopericytoma and angioleiomyoma. RGS5 expression was also found in cases of glomus tumor meeting the histologic criteria for malignancy. In contrast, more limited RGS5 expression was observed in myofibroma, solitary fibrous tumor and PEComa family tumors. RGS5 expression may demonstrate clinical utility for the evaluation of pericytic differentiation in soft tissue tumors, in combination with αSMA, CD146, and PDGFRβ.

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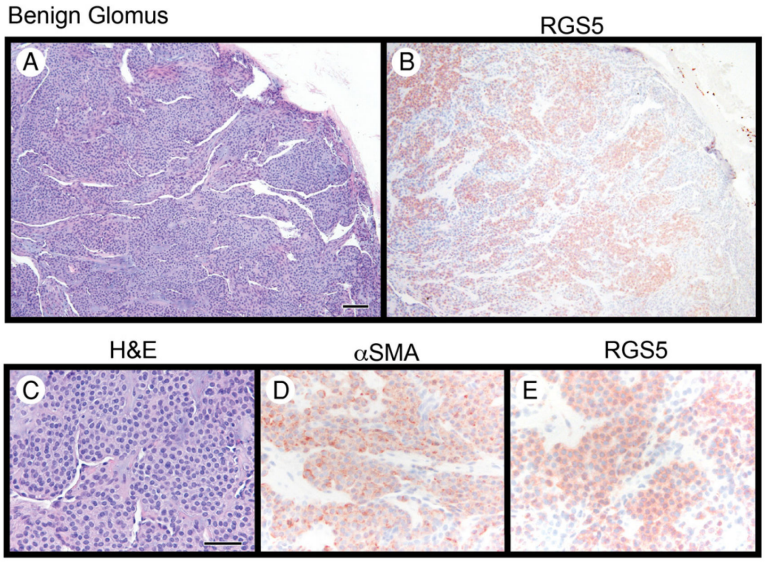

Fig. 1.

RGS5 expression in glomus tumor. A, Histological appearance of glomus tumor, by routine H&E staining. B, RGS5 expression in a typical glomus tumor. C–E, Appearance of solid glomus tumor, including H&E (C), αSMA (D), and RGS5 (E) immunohistochemical staining. Black scale bar: 50 μm.

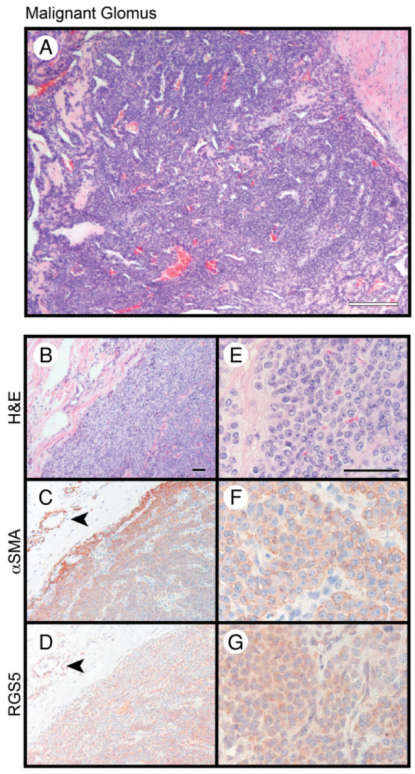

Fig. 2.

RGS5 expression in malignant glomus tumor. A, Histological appearance of malignant glomus tumor, by routine H&E staining. B–D, Edge of malignant glomus tumor and adjacent non-lesional vessels (black arrowheads), including H&E (B), αSMA (C), and RGS5 immunohistochemical staining (D). E–G, High magnification images of malignant glomus tumor, including H&E (E), αSMA (F), and RGS5 (G) immunohistochemical staining. Black scale bar: 50 μm. White scale bar: 200 μm.

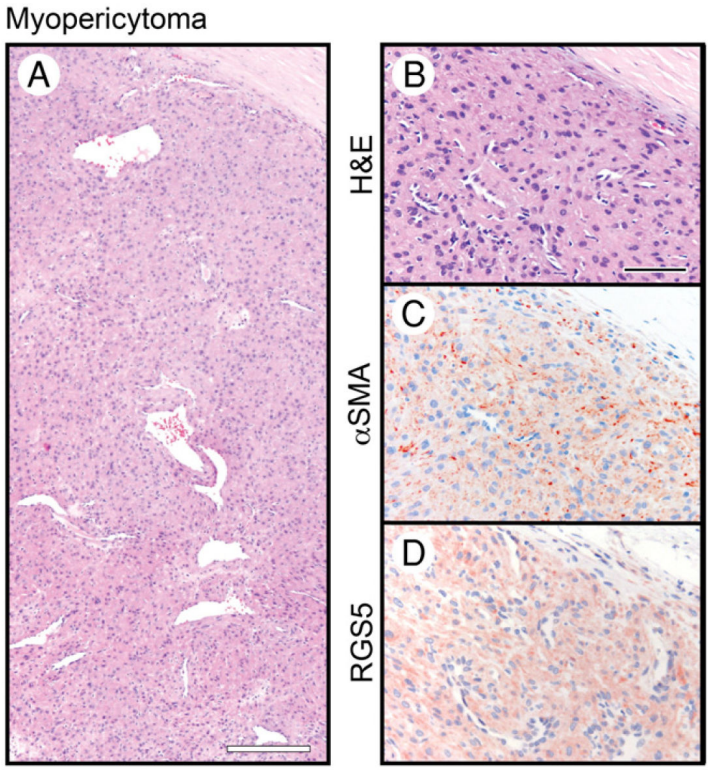

Fig. 3.

RGS5 expression in myopericytoma. A, Histological appearance of myopericytoma, by routine H&E staining. B–D, Edge of myopericytoma, including H&E (B), αSMA (C), and RGS5 (D) immunohistochemical staining. Black scale bar: 50 μm. White scale bar: 200 μm.

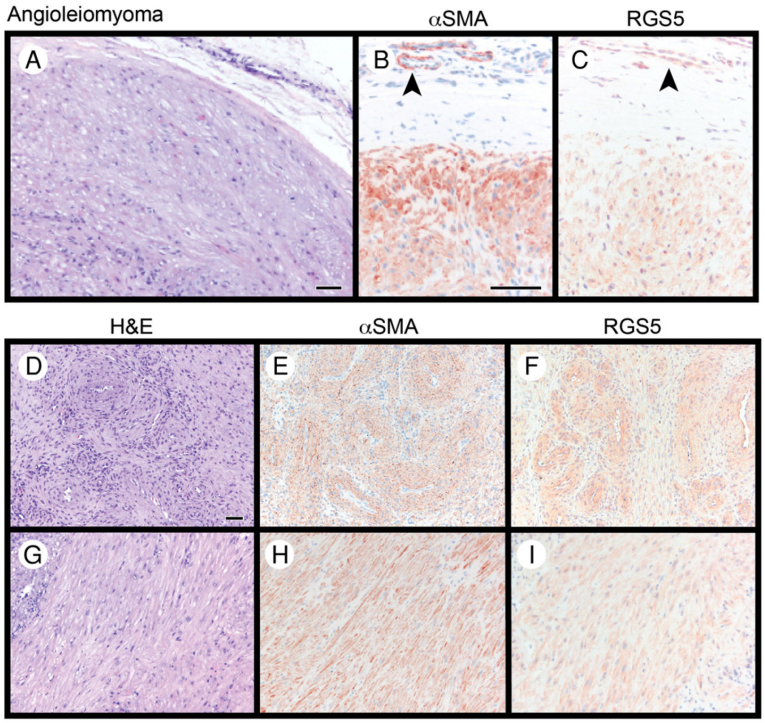

Fig. 4.

RGS5 expression in angioleiomyoma. A, Histological appearance of angioleiomyoma, by routine H&E staining. B and C, Edge of angioleiomyoma and adjacent non-lesional vessels (arrowheads), including αSMA (B) and RGS5 immunohistochemical staining (C). D–F, Venous growth pattern in angioleiomyoma, including H&E staining (D), αSMA (E), and RGS5 immunohistochemical staining (F). G–I, Fascicular growth pattern in angioleiomyoma, including H&E staining (G), αSMA (H), and RGS5 (I) immunohistochemical staining. Black scale bar: 50 μm.

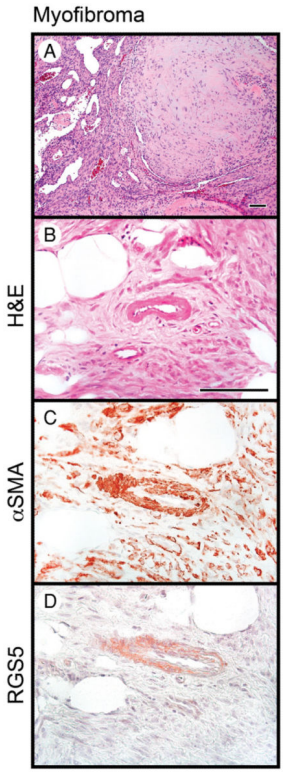

Fig. 5.

RGS5 expression in myofibroma. A, Histological appearance of myofibroma, by routine H&E staining. A characteristic zonal appearance was seen, with myoid nodules with chondromyxoid matrix (right) accompanied by more cellular “myopericytomous” areas with thin walled, branching blood vessels (left). B–D, Typical appearance of myofibroma, including H&E (B), αSMA (C), and RGS5 (D) immunohistochemical staining. Immunoreactivity for RGS5 is predominantly limited to the intratumoral vessels. Black scale bar: 100 μm.

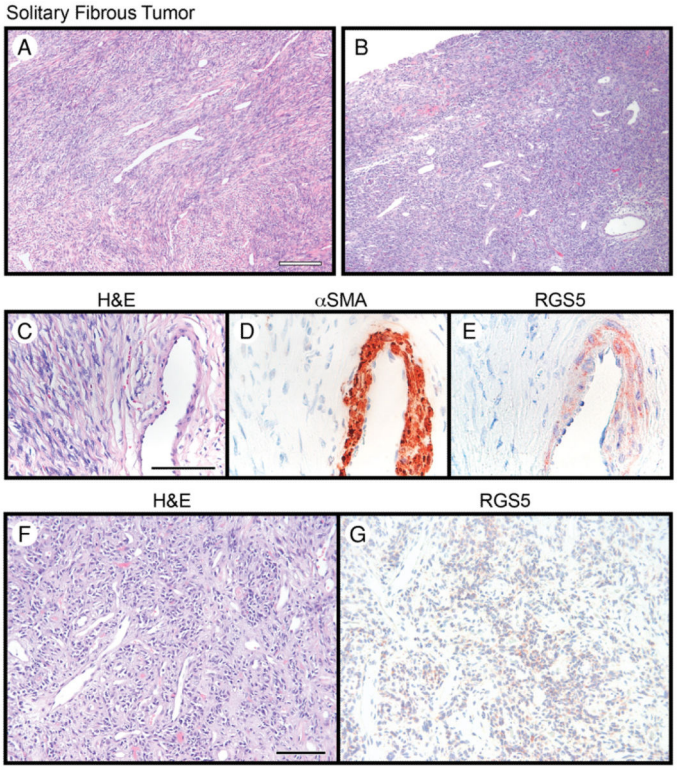

Fig. 6.

RGS5 expression in SFT. A and B, Histological appearance of solitary fibrous tumor, by routine H&E staining. A spectrum of morphologic findings were seen, from more spindled cells set in a fibrous stroma (A) to more plump ovoid cells more consistent with "hemangiopericytoma"-like features (B). C–E, Typical appearance of solitary fibrous tumor, including H&E (C), αSMA (D), and RGS5 (E) immunohistochemical staining. Immunoreactivity for SMA and RGS5 is essentially limited to the intratumoral vessels in some cases. F and G, Limited RGS5 immunoreactivity in some cases. Black scale bar: 50 μm. White scale bar: 200 μm.

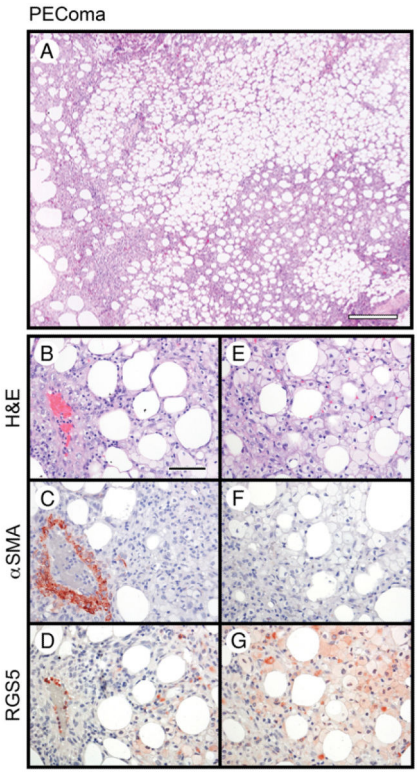

Fig. 7.

RGS5 Expression in PEComa. A and B, Histological appearance of a typical angiomyolipoma, by routine H&E staining. B–D, Typical appearance of angiomyolipoma, including H&E (B), αSMA (C), and RGS5 immunohistochemical staining (D). Strong immunoreactivity for RGS5 is commonly limited to the intratumoral vessels. E–G, Focal RGS5 immunoreactivity in some cases, including H&E (E), αSMA (F), and RGS5 (G) immunohistochemical staining. Black scale bar: 50 μm. White scale bar: 200 μm.

Table 1

Summary of RGS5 expression in various perivascular tumor types. Expressed as mean ± SD

Tumor type	RGS5 intensity	RGS5 distribution (%)
Glomus tumor	2.17 (±0.75)	68.33 (±25.23)
Malignant glomus tumor	2.25 (±0.5)	58.75 (±10.31)
Myopericytoma	2 (0)	96.67 (±5.77)
Angioleiomyoma	1.78 (±0.97)	81.67 (±31.22)
Myofibroma	0.5 (±1.0)	1.25 (±2.5)
Solitary fibrous tumor	1 (±0.67)	26.5 (±25.06)
PEComa	0.68 (±0.67)	10 (±13.02)

Abbreviation: PEComa, perivascular epithelioid cell tumor.

Table 2

Tumor demographic and RGS5 expression for each individual tumor

Sample #	Diagnosis	Gender (M/F)	Age (y)	Location	Size (cm)	RGS5 intensity	RGS5 distribution (%)
1	Glomus tumor	M	52	Thumb	0.8	2+	75
2	Glomus tumor	F	42	Fifth finger	0.4	3+	90
3	Glomus tumor	M	47	Fifth finger	0.4	2+	75
4	Glomus tumor	F	58	Ring finger	0.8	1+	65
5	Glomus tumor	F	51	Thumb	0.5	2+	20
6	Glomus tumor	F	43	Ring finger	0.5	3+	85
7	Malignant glomus tumor	F	55	Forearm	5.5	2+	65
8	Malignant glomus tumor	F	56	Forearm	Unk	3+	50
9	Malignant glomus tumor	F	55	Paraspinal	4.5	2+	50
10	Malignant glomus tumor	M	30	Stomach	5.1	2+	70
11[a]	Myopericytoma	M	76	Knee	3.0	2+	100
12[a]	Myopericytoma	M	76	Knee	3.0	2+	100
13	Myopericytoma	F	60	Foot	0.9	2+	90
14	Angioleiomyoma	M	46	Ankle	1.5	0	0
15	Angioleiomyoma	F	52	Knee	1.5	2+	100
16	Angioleiomyoma	F	34	Index finger	0.8	2+	90
17	Angioleiomyoma	M	47	Knee	2.0	1+	80
18	Angioleiomyoma	F	48	Knee	2.5	2+	90
19	Angioleiomyoma	F	68	Knee	1.1	1+	90
20	Angioleiomyoma	F	59	Palm	0.7	3+	90
21	Angioleiomyoma	F	59	Ankle	1.4	2+	95
22	Angioleiomyoma	M	29	Index finger	1.3	3+	100
23	Myofibroma	F	80	Chest wall	2.8	0	0
24	Myofibroma	F	57	Thigh	12.6	0	0
25	Myofibroma	F	60	Buttock	8.0	2+	5
26	Myofibroma	M	41	Lower leg	2.0	0	0
27	SFT	M	61	Retromaxilla	1.6	0	0
28	SFT	M	69	Pelvis	4.5	1+	10
29	SFT	F	40	Pleura	7.8	1+	15
30	SFT	F	18	Upper arm	3.5	0	0
31	SFT	F	65	Intra abdominal	Unk	2+	65
32	SFT	F	54	Thigh	2.2	1+	60
33	SFT	F	94	Thigh	Unk	1+	20
34	SFT	F	49	Groin	4.0	1+	5
35	Atypical SFT	F	89	Maxilla	1.8	2+	50
36	Atypical SFT	M	24	Thigh	6.0	1+	40
37	AML	F	49	Renal	6.9	1+	5
38	AML	F	48	Retroperitoneal	11.3	0	0
39	AML	F	53	Renal	5.5	0	0

Sample #	Diagnosis	Gender (M/F)	Age (y)	Location	Size (cm)	RGS5 intensity	RGS5 distribution (%)
40	AML	F	42	Renal	3.0	2+	30
41	AML	F	49	Renal	7.8	0	0
42	AML	F	29	Renal	5.0	1+	5
43	AML	M	66	Renal	5.0	2+	5
44	AML	F	80	Renal	10.5	0	0
45	AML	M	67	Renal	2.3	0	0
46	AML	F	82	Renal	1.1	1+	10
47	AML	F	55	Renal	2.0	1+	35
48	AML	M	86	Renal	3.6	1+	40
49	AML	F	46	Retroperitoneal	13.0	0	0
50	AML	F	48	Liver	Unk	1+	10
51	AML	F	29	Renal	3.5	1+	15
52	Malignant PEComa	F	38	Renal	10.0	1+	10
53	Lymphangiomyoma	F	46	Mediastinal	8.0	0	0
54	Lymphangiomyoma	F	88	Pelvis	2.0	0	0
55	Lymphangiomyoma	F	37	Pelvis	2.6	1+	25

Abbreviations: AML, angiomyolipoma; F, female; M, male; PEComa, perivascular epithelioid cell tumor; SFT, solitary fibrous tumor; Unk, unknown.

[a]Samples 11 and 12 represent biopsy and resection specimens from the same patient.