Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Study Design

1. Study design and participants.

This study was approved by the medical ethics review board of the University of Louvain. We retrospectively collected archived samples from 102 patients from clinical centers in Belgium, France, the USA and the Netherlands (the Dutch nationwide population-based pathology database (PALGA), Houten, The Netherlands[1]), diagnosed with sporadic myofibroma, myopericytoma, or myofibromatosis according to the WHO classification. One patient was included prospectively after diagnosis and informed consent of the parents. The diagnosis of 91 patients was confirmed by one of the pathologists who participated in our study. In addition, the haematoxylin- and eosin-stained slides of lesions from 78 patients from Belgium and the Netherlands underwent central pathology review to confirm diagnoses. Smooth muscle actin staining was reassessed as well, when available. This led to the exclusion of 12 samples from 12 different patients. Among these, seven had dubious diagnoses (one normal skin and six histological patterns non-compatible with myofibroma) and five were not further investigated because of low quality extracted DNA (*vide infra*). We extracted DNA from fresh frozen or formalin-fixed paraffin-embedded (FFPE) tissue and performed a double quality check based on (1) DNA quality after extraction and (2) quantification of sequencing-libraries by real time PCR, excluding samples from 21 additional patients, and finally retaining 85 samples from 69 patients, 16 of which had been previously described[2].

2. Targeted next generation sequencing and data analysis

We used three different Ion AmpliSeq (IA) Custom DNA Panels (ThermoFisher Scientific, USA): Panel IA1 to sequence *PDGFRB* (coding exons with at least 10 nucleotides of flanking introns) on DNA from frozen samples (100% exon coverage); IA2 for *PDGFRB* (coding exons with at least 10 nucleotides of flanking introns) on DNA from formalin-fixed paraffin-embedded tissue (95.35% exon coverage); and IA3 for the whole *PDGFRB* gene (chr5: 149493402-149535927), including the promoter, introns and UTRs (95.35% gene coverage) on DNA from frozen tissue. Genomic DNA was extracted from frozen cells (QIAamp DNA Blood Mini Kit, Qiagen, Hilden, Germany), frozen tissues (DNeasy Blood & Tissue Kit, Qiagen) or formalin-fixed paraffin-embedded (FFPE) tissues (QIAamp DNA FFPE Tissue Kit, Qiagen), as described[2]. Libraries were prepared from at least 10 ng of DNA with Ion AmpliSeq Library kit 2.0 (ThermoFisher Scientific, Publication MAN0006775, Revision C.0) with one of the three custom-designed panel of AmpliSeq primers (IA1, IA2 or IA3). DNA libraries were purified with Agencourt AMPure XP kit (Beckman Coulter, Indianapolis, Indiana). Libraries were quantified using real time PCR with Ion Library TAQMAN Quantitation kit, allowing for optimal final dilution for template preparation. Libraries at concentration below 50 pM were excluded. Emulsion PCR was carried out using the Ion PGM™ Hi-Q™ OT2 Kit on a OneTouch 2 System (both from Life Technologies) according to manufacturer's protocol (Ion PGM™ Hi-Q™ OT2 Kit, Publication MAN0010902, Revision A.0). Prepared templates (bead-bound DNAs) were loaded onto an Ion 316™ Chip V2, and sequenced using the Ion PGM™ Hi-Q™ Sequencing Kit on an Ion PGM (all from Life Technologies; protocol in Publication MAN0014583, Revision C.0). Sequences were generated in the form of FASTQ files, and alignment was performed with TMAP 5.6.0 (https://github.com/iontorrent/TMAP) and variant calling with Torrent Variant Caller 5.8.0 (https://github.com/iontorrent/Torrent-Variant-Caller-stable). The mean exon coverage depth was >2200 x. Annotation and analyses were performed with Highlander (Helaers R. and Vikkula M., https://sites.uclouvain.be/highlander/). We used the following criteria to select candidate

variants: >500 total number of reads covering the position; present at <1‰ frequency in public sequence databases (GoNL, ExAC), and ≥4% allelic depth proportion. Visual curation was used to discard artifacts such as variants located in homopolymers. Variants called based on this filtering strategy are described in eTable 1. We inspected manually highly recurrent genomic positions, i.e. PDGFRB: c.1997 & 1998 (corresponding to PDGFRB:p.N666), PDGFRB:c.1681 (corresponding to PDGFRB:p.R561), PDGFRB:c.2548 (corresponding to PDGFRB:p.D850) and PDGFRB:c.1615 (corresponding to PDGFRB:p.I538) to avoid missing common variant. This led to the identification of one variant affecting patient 48 (PDGFRB:p.N666S). Samples carrying ≥5 variants per kilobase based on the mentioned criteria (*vide supra*) were submitted to more stringent variant-filtering: ≥7% allelic depth proportion, and predicted to affect protein function by ≥ 2 softwares.

The analysis of the sequencing results revealed a heavy mutational load with a high proportion of C>T or G>A substitutions in 28 samples. These are typical artefacts of DNA extracted from FFPE samples. Importantly, the rate of clinically relevant PDGFRB mutations identified in FFPE samples was similar to that of frozen samples (eTable 1). In FFPE samples from patients 19, 46 and 96, we could not pinpoint candidate (potential true-positive) variants with our filtering strategy, and we considered these samples negative. This may have resulted in a slight underestimation of the proportion of *PDGFRB* mutated samples in our cohort.

We proceeded as follows to identify putative heterozygous germline variants, based on their expected allelic fraction of 50%. We used known heterozygous polymorphisms to calculate the experimental allelic fraction range corresponding to germline variations in our sequencing experiments. We first identified heterozygous single nucleotide polymorphisms (SNP) present in our sequencing results of two patients for which we obtained tumor and matched normal samples, using the following criteria: present at ≥ 5% frequency in public sequence databases (GoNL[3] or ExAC[4]), and allelic proportion >10%. This enabled us to calculate the mean of the measured allelic proportion of heterozygous SNP (49.46% ± 4.03%). We considered variants with allelic proportions that were within one standard deviation as "likely to be germline". This led us to pinpoint three PDGFRB variants (affecting patients 14, 41 and 48), mentioned in the Results section, in eTable 1 and illustrated in Figure 2.

3. Copy-number variation analysis

We performed multiplex ligation-dependent probe amplification (MLPA)[5] using the SALSA MLPA probemix P500-X1-0614 (MRC Holland, The Netherlands) with three additional synthetic probes targeting *PDGFRB*. The Fluorescein-amidite labeled PCR products were separated by capillary electrophoresis on an ABI-3130XL device (Applied Biosystems, California, USA). The size standard was the Internal Lane Standard 600 (ILS 600) (Promega, Wisconsin, USA). We carried out this experiment on 30 samples but we kept only 12 samples presenting at least one fragment MLPA reaction score bar for comparative analysis. We analyzed peak intensities using Coffalyser.net software (MRC-Holland).

Probe sequences:

- Probe targeting PDGFRB exon 8:
    - Left probe oligo: 5'-GGGTTCCCTAAGGGTTGGACCACTACACCATGCGGGCCTTCCATGAGGATGCT-3'

    - Right probe oligo: 5'-GAGGTCCAGCTCTCCTTCCAGCTACAGATCAATGTCTAGATTGGATCTTGCTGGCAC-3'
- Probe targeting PDGFRB exon 6:
    - Left probe oligo: 5'-GGGTTCCCTAAGGGTTGGAGAAGACTCGGGGACCTACACCTGCAATGTGACGGAGAGT-3'
    - Right probe oligo: 5'-GTGAATGACCATCAGGATGAAAAGGCCATCAACATCACTCTAGATTGGATCTTGCTGGCAC-3'
- Probe targeting PDGFRB exon 22:
    - Left probe oligo: 5'-GGGTTCCCTAAGGGTTGGAGGACACCAGCTCCGTCCTCTATACTGCCGTGCAG-3'
    - Right probe oligo: 5'-CCCAATGAGGGTGACAACGACTATATCATCCCCCTGCCTTCTAGATTGGATCTTGCTGGCAC-3'

4. Allele-specific PCR and Sanger sequencing

Selected mutations were confirmed using allele-specific PCR as previously described[2], or PCR-cloning in pcDNA™ 3.1/V5-His TOPO® (according to the manufacturer's protocol; ThermoFisher Scientific, USA) followed by Sanger sequencing of multiple clones. We established that double mutations were in cis by producing cDNA (when RNA was available, i.e. patient 13) followed by PCR-amplification of a region containing both variants, cloning and Sanger sequencing of multiple clones. Alternatively, when mutations were located in the same exon, we amplified genomic DNA, cloned the PCR product and performed Sanger sequencing.

5. Site-directed mutagenesis and functional assays in transiently transfected cells.

The mutations p.Y562D, p.Y562_V572dup, p.V504_R505_insLLSV, p.R561_Y562delinsH, and p.A537D_I538N were introduced into full length human *PDGFRB* coding sequence (RefSeq NM_002609) cloned in pcDNA3.1 (ThermoFischer Scientific, California, USA) according to the QuickChange XL-II kit protocol (Agilent, California, USA). We verified every construct by sequencing.

MCF7 and PAE cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM, Gibco, Life Technologies) supplemented with 10% fetal bovine serum (FBS) and antibiotics (50 U/ml penicillin and 50 µg/ml streptomycin).

Luciferase assays

To monitor mitogen-activated protein kinases (MAPK) activation, MCF7 cells were seeded in 12- or 24-well plates (120 000 or 55 000 cells/well) for 24 hours. Cells were transiently co-transfected with three different constructs: a wild-type (WT) or mutated receptor, a β-galactosidase reporter and a luciferase gene cloned downstream of a serum-response elements promoter (pSRE-luc), using TurboFect™ Transfection Reagent (ThermoFischer

Scientific). Four hours after transfection, cells were treated or not with imatinib for 20 hours (final concentration of 500 nM). Twenty-four hours after transfection, cells were lysed and the luciferase activity was assessed as described[6] by using GloMax© (Promega, Leiden, The Netherlands).

To monitor the activation of signal transducers and activators of transcription (STAT), PAE cells were seeded in 24-well plates (55 000 cells/well) for 24 hours. Then, cells were transiently co-transfected with 3 different constructs: a wild-type (WT) or mutated receptor, a pGGR5-luc reporter and a β-galactosidase control reporter, using TurboFect™ Transfection Reagent (ThermoFischer Scientific). Four hours after transfection, cells were washed with PBS and starved in minimum essential medium supplemented with 0.05% bovine serum albumin, 50 U/ml penicillin, 50 µg/ml streptomycin and 2 mM glutamine. Cells were then treated or not with imatinib for 20 hours (final concentration of 500 nM). Twenty-four hours after transfection, cells were lysed and the luciferase activity was assessed as described[6] by using GloMax©.

The β-galactosidase activity was assessed by mixing 40 µl of lysate with 40 µl of substrate solution (165 mM Na_2HPO_4, 38 mM NaH_2PO_4, 2 mM $MgCl_2$, 72 mM β-mercaptoethanol, 4.4 mM o-nitrophenyl-β-D-galactopyranoside) and by measuring the absorbance at 405 nm after 30 min.

6. Statistical analysis

Statistical analysis was computed in R and Excel. We considered two-sided P-values <0.05 to be significant. We performed all cellular experiments at least three times. Statistical analyses of the luciferase assays were performed using Student's bilateral t-test (*, $p<0.05$; **, $p<0.01$; ***, $p<0.001$).

eTable 1. Called Variants Related to Patients and Samples

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eTable 1 reports variants called after using targeted next generation sequencing of *PDGFRB* on archived myofibroma samples. DNA was extracted from fresh frozen or formalin-fixed paraffin-embedded (FFPE) tissue.

Filtering criteria of the called variants were the following:

>500 total number of reads covering the position; present at <1‰ frequency in public sequence databases (GoNL, ExAC), and≥4% allelic depth proportion. Visual curation was used to discard likely artifacts such as variants located in homopolymers.

Samples carrying ≥5 variants per kilobase based on these criteria were submitted to more stringent variant-filtering: ≥7% allelic depth proportion, and predicted to affect protein function by ≥ 2 software. These samples are marked with a "§".

eTable 1 describes:

- patient identification number
- sex and age of the patient
- Solitary (0) or multicentric (1) status of the disease
- sample code (when multiple samples from the same patient were analyzed
- type of sample (FFPE or fresh-frozen)
- HGVS nomenclature of the variant, at the protein and the DNA level
- allelic depth fraction of the variant (= percentage of mutant reads)
- method of molecular validation of the variant: IT (variant confirmed by another run of NGS by IonTorrent), AS (Allele-specific PCR), Sanger (Sanger sequencing after cloning).

NB:

1. It is worth noting that, owing to the lack of clinical details for some archived cases, the number of multifocal cases as well as recurrence rate may be underestimated.
2. Samples highlighted in red are healthy tissue used as controls. These were not taken into account in the total number of myofibroma samples (*i.e.* 85 samples)
3. Patients annotated with ‡ died from their disease.

Patient ID	Sex	Age	Multicentric disease	Lesion localization	DNA origin	hgvs protein	hgvs dna	allelic depth proportion	Molecular Validation	Sequencing code
2	F	0	1	Thigh	FFPE	p.Asp850Val	c.2549A>T	8%		CAFSARC-64.pPDGFRBCDS
				Thigh	Fresh frozen	p.Asp850Val	c.2549A>T	8%	AS PCR + IT	CAFSARC-11.pPAPBKIT, CAFSARC-2.pPAPBKIT, CAFSARC20.pPBTOTN3
				Blood (control)	Fresh frozen					CAFSRAC-17.pPAPBKIT, CAFSARC23.pPBTOTN3
3	M	0	1	NA (muscular or subcutaneous)	Fresh frozen					CAFSARC-3.pPAPBKIT
4 ‡	M	0	1	Multicentric, not otherwise specified	Fresh frozen					CAFSARC-4.pPAPBKIT
6	M	0	0	cutaneous, back	Fresh frozen					CAFSARC-6.pPAPBKIT
7	F	7	1	Rib, bone lesion	FFPE	p.Asn666Lys	c.1998C>A	14%		CAFSARC-60.pPDGFRBCDS
				Paraspinal (right)	FFPE	p.Tyr562Asp	c.1684T>G	17%	AS PCR	CAFSARC-62.pPDGFRBCDS
				Deltoid muscle	Fresh frozen	p.Asn666Lys	c.1998C>G	16%		CAFSARC-10.pPAPBKIT, CAFSARC19.pPBTOTN3, CAFSARC-7.pPAPBKIT
				Rib, bone lesion	Fresh frozen	p.Asn666Lys	c.1998C>A	20%	AS PCR + IT	CAFSARC-15.pPAPBKIT, CAFSARC21.pPBTOTN3
				Occipital region, cutaneous Naevus	Fresh frozen FFPE	p.Trp566_Val568delinsLeu	c.1697_1702delGGAAGG	6%	AS PCR + IT	CAFSARC-16.pPAPBKIT, CAFSARC22.pPBTOTN3 CAFSARC27.pPDGFRBCDS
				Healthy tissue around the naevus (con	FFPE					CAFSARC28.pPDGFRBCDS
9	F	6	0	Foot	Fresh frozen					CAFSARC12.pPAPBKIT
10	M	6	0	Foot	Fresh frozen					CAFSARC13.pPAPBKIT
13	M	4	1	Cutaneous, shoulder	FFPE	p.Asn666Lys ; p.Trp566Arg	c.1998C>A ; c.1696T>C	21% ; 18%	Sanger + AS PCR + IT (in *cis*)	CAFSARC33.pPDGFRBCDS
				cutaneous, neck	FFPE	p.Asn666Lys ; p.Trp566Arg	c.1998C>A ; c.1696T>C	17% ; 12%	Sanger + AS PCR + IT (in *cis*)	CAFSARC34.pPDGFRBCDS
				Multicentric, cutaneous	Fresh frozen	p.Asn666Lys ; p.Trp566Arg	c.1998C>A ; c.1696T>C	28% ; 10%	Sanger + AS PCR + IT (in *cis*)	CAFSARC-18.pPAPBKIT, CAFSARC24.pPBTOTN3
14	M	0	1	Multicentric: Skull, Arm, Spleen	FFPE	p.Arg561Cys ; p.Asn666Lys	c.1681C>T ; c.1998C>A	46% ; 16%	Sanger	CAFSARC32.pPDGFRBCDS
15	M	4	0	Mandibular region	FFPE			13%		CAFSARC-35.pPDGFRBCDS, CAFSARC-39.pPDGFRBCDS
16	M	1	1	multicentric, near mandibular gland	FFPE	p.Ile538_Leu539insArg	c.1615_1616insGAT	20%	AS PCR	CAFSARC-40.pPDGFRBCDS
				multicentric, mandibula	FFPE	p.Ile538_Leu539insArg	c.1615_1616insGAT	15%	AS PCR	§ CAFSARC-41.pPDGFRBCDS
				multicentric, mandibula (recurrence)	Fresh frozen	p.Ile538_Leu539insArg	c.1615_1616insGAT	24%	AS PCR	CAFSARC-37.pPBTOTN3
17	F	2	0	skull	FFPE	p.Ile538_Leu539insArg	c.1615_1616insGAT	14%	AS PCR	§ CAFSARC-42.pPDGFRBCDS
18	M	45	0	Thigh	FFPE					CAFSARC-43.pPDGFRBCDS
19	M	24	0	tongue	FFPE					§ CAFSARC-44.pPDGFRBCDS
21	F	0	1	NA	FFPE	p.Asp850Val	c.2549A>T	32%	AS PCR	CAFSARC-46.pPDGFRBCDS
22	M	44	0	Finger	FFPE					CAFSARC-47.pPDGFRBCDS
23	M	31	0	Shoulder	FFPE					CAFSARC-48.pPDGFRBCDS
24	F	50	0	Cutaneous, not otherwise specified	FFPE					CAFSARC-49.pPDGFRBCDS
25	F	2	0	Arm	FFPE	p.Ile538_Leu539insArg	c.1615_1616insGCC	9%		CAFSARC-50.pPDGFRBCDS
26	F	49	0	Finger	FFPE					CAFSARC-51.pPDGFRBCDS
28	F	15	0	Forehead	FFPE					CAFSARC-53.pPDGFRBCDS
29	M	43	0	Finger	FFPE					CAFSARC-54.pPDGFRBCDS
30	F	13	0	left leg, cutaneous	FFPE					CAFSARC-55.pPDGFRBCDS
31	M	28	0	NA	FFPE					CAFSARC-56.pPDGFRBCDS
32	M	0	0	Cauda equina	Fresh frozen	p.Tyr562_Val572dup	c.1716_1717ins GAGCTGATCCGATGGAAGGTGATTGAGTCTGTG	38%	AS PCR	CAFSARC-57.pPBTOTN3
34	F	12	0	Forehead	FFPE					CAFSARC-65.pPDGFRBCDS
36	M	0	0	Cutaneous, not otherwise specified	FFPE					CAFSARC-67.pPDGFRBCDS

Patient ID	Sex	Age	Multicentric disease	Lesion localization	DNA origin	hgvs_protein	hgvs_dna	allelic_depth_proportion	Molecular Validation	Sequencing code
37	F	0	1	Multicentric, cutaneous	FFPE	p.Asn666Ser	c.1997A>G	32%		CAFSARC-68.pPDGFRBCDS
38	F	9	0	Cutaneous, not otherwise specified	FFPE					CAFSARC-69.pPDGFRBCDS
39	F	2	0	Cutaneous, not otherwise specified	FFPE					CAFSARC-70.pPDGFRBCDS
41	M	0	1	Multicentric, cutaneous	FFPE	p.Arg561_Tyr562delinsHis ; p.Asn666Lys	c.1682_1684delGTT ; c.1998C>G	51% ; 21%		CAFSARC-72.pPDGFRBCDS
43	F	9	0	Cutaneous, not otherwise specified	FFPE					CAFSARC-74.pPDGFRBCDS
44	M	9	0	Cutaneous, solitary	FFPE	p.Ile538_Leu539insArg	c.1615_1616insGAT	22%		CAFSARC-75.pPDGFRBCDS
45	M	0	1	Generalized	FFPE	p.Tyr562_Arg565del ; p.Asn666Lys	c.1683_1694delTTACGAGATCCG ; c.1998C>A	31% ; 30%		CAFSARC-76.pPDGFRBCDS
46	M	0	0	Cutaneous, solitary	FFPE					CAFSARC-77.pPDGFRBCDS
48	F	0	1	Multicentric, cutaneous	FFPE	p.Arg561Cys ; p.Asn666Ser	c.1681C>T ; c.1997A>G	52% ; 30%	Sanger (p.N666S)	CAFSARC-79.pPDGFRBCDS
49 ‡	F	0	1	lung (left) lung (right) heart Stomach Liver adrenal gland (right)	FFPE FFPE FFPE FFPE FFPE FFPE					CAFSARC-81.pPDGFRBCDS CAFSARC-83.pPDGFRBCDS CAFSARC-84.pPDGFRBCDS CAFSARC-85.pPDGFRBCDS CAFSARC-86.pPDGFRBCDS CAFSARC-87.pPDGFRBCDS
50	M	0	1	back	FFPE	p.Asp850Tyr	c.2548G>T	34%		CAFSARC-PALGA-1.pPDGFRBCDS
52	F	0	0	Cutaneous, Thorax	FFPE					CAFSARC-PALGA-4.pPDGFRBCDS
55	F	0	0	Mandibula	FFPE					CAFSARC-PALGA-7.pPDGFRBCDS
57	F	0	1	Jejunal mesentery	FFPE					CAFSARC-PALGA-9.pPDGFRBCDS
59	F	0	0	Muscular, Nek	FFPE					CAFSARC-PALGA-11.pPDGFRBCDS
61	M	0	1	Subscapular region	FFPE					CAFSARC-PALGA-13.pPDGFRBCDS
62	F	0	1	Multicentric, jejunum and cutaneous	FFPE					CAFSARC-PALGA-15.pPDGFRBCDS
63	F	0	0	ano-rectal region	FFPE					CAFSARC-PALGA-16.pPDGFRBCDS
73	M	13	0	boe, lytic lesion	FFPE	p.Ile538_Leu539insArg	c.1615_1616insGAT	12%		CAFSARC-PALGA-25.pPDGFRBCDS
74	F	1	0	Cutaneous, Skull	FFPE					CAFSARC-PALGA-26.pPDGFRBCDS
75	F	10	0	Cutaneous, Nek	FFPE					CAFSARC-PALGA-27.pPDGFRBCDS
77	NA	NA	0	Cutaneous, Nek	FFPE					CAFSARC-PALGA-28.pPDGFRBCDS
79	F	6	0	cutaneous, lower back	FFPE	p.Ala537Asp ; p.Ile538Asn	c.1610C>A ; c.1613T>A	7% ; 7%	Sanger (in *cis*)	CAFSARC-PALGA-30.pPDGFRBCDS
80	F	10	0	cutaneous, mandibular region	FFPE					CAFSARC-PALGA-32.pPDGFRBCDS
81	M	1	0	Nek	FFPE					CAFSARC-PALGA-34.pPDGFRBCDS
84	F	7	0	Mouth, mucous membrane	FFPE	p.Ile538_Leu539insArg	c.1615_1616insGAT	11%		§ CAFSARC-PALGA-37.pPDGFRBCDS
85	F	4	1	multicentric myopericytoma, cutaneou	FFPE	p.Lys559_Tyr562delinsAsn	c.1677_1685delGCCACGTTA	44%	Sanger (p.Lys559_Tyr562delinsAsn)	CAFSARC-PALGA-41.pPDGFRBCDS
	F	4	1	multicentric myopericytoma, lung	FFPE	p.Asn666Lys	c.1998C>A	27%		CAFSARC-PALGA-38.pPDGFRBCDS
86	M	0	0	Cutaneous, Thorax	FFPE					CAFSARC-PALGA-39.pPDGFRBCDS
87	F	0	0	Thorax, cutaneous	FFPE					CAFSARC-PALGA-40.pPDGFRBCDS
90	M	0	0	subcutaneous, tibial region	FFPE	p.Trp566Arg ; p.Tyr589Asp	c.1696T>A ; c.1765T>G	27% ; 26%	Sanger (in cis)	CAFSARC-PALGA-43.pPDGFRBCDS
92	F	0	1	Multicentric, cutaneous	FFPE	p.Arg561Cys	c.1681C>T	28%	Sanger	§ CAFSARC-PALGA-45.pPDGFRBCDS
93	M	7	0	Back	FFPE					CAFSARC-PALGA-46.pPDGFRBCDS
95	M	9	0	cutaneous, forehead	FFPE					CAFSARC-PALGA-48.pPDGFRBCDS

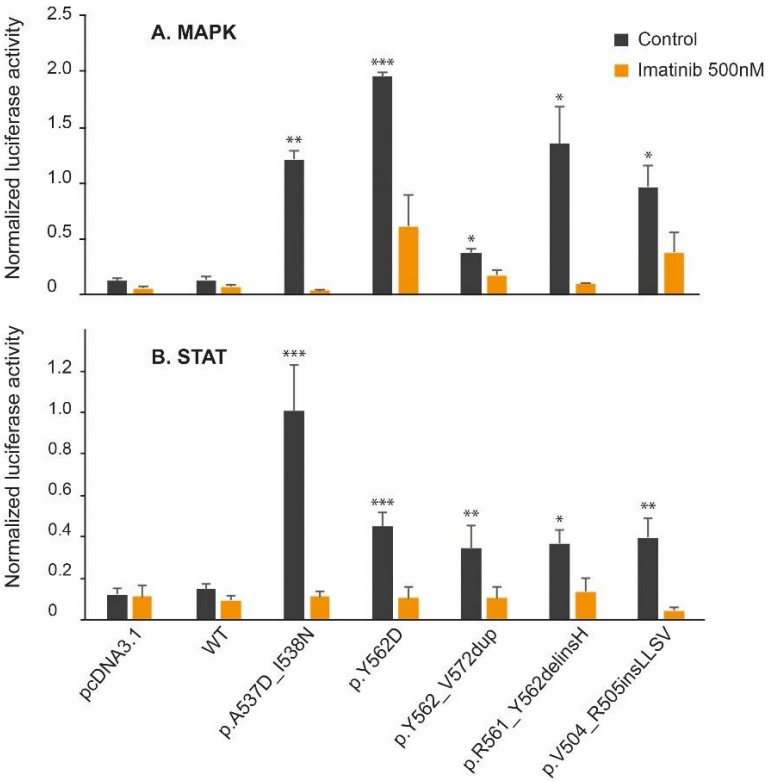
Patient ID	Sex	Age	Multicentric disease	Lesion localization	DNA origin	hgvs_protein	hgvs_dna	allelic_depth_proportion	Molecular Validation	Sequencing code
96	M	2	0	Forehead, cutaneous	FFPE					§ CAFSARC-PALGA-49.pPDGFRBCDS
101	M	1	0	Cutaneous,nose	FFPE	p.Val506_Arg507insLeuLeuSerVal	c.1519_1520insTACTGTCGGTGC	18%	Sanger	§ CAFSARC-PALGA-54.pPDGFRBCDS
102	M	10	0	lower back, cutaneous	FFPE	p.Asn666Lys ; p.Trp566Gly	c.1998C>A ; c.1696T>G	39% ; 17%		CAFSARC-PALGA-55.pPDGFRBCDS
103	M	1	0	thorax, cutaneous	FFPE	p.Arg561Cys ; p.Asn666Lys	c.1681C>T ; c.1998C>A	22% ; 20%		CAFSARC-PALGA-56.pPDGFRBCDS
104	M	4	0	Shoulder	FFPE					CAFSARC-PALGA-57.pPDGFRBCDS
105	M	6	0	Cutaneous, Skull	FFPE					CAFSARC-PALGA-58.pPDGFRBCDS
106	F	11	0	Cutaneous, Thorax	FFPE					CAFSARC-PALGA-59.pPDGFRBCDS
107	M	0	0	lower back, cutaneous	FFPE					CAFSARC-PALGA-61.pPDGFRBCDS
108	F	3	0	finger	FFPE					CAFSARC-PALGA-62.pPDGFRBCDS

eTable 2. Clinical Characteristics of Patients Harboring a *PDGFRB* Mutation

Patient features	n (%)
Patients included	25 (100)
Sex	
Female	12 (48)
Male	13 (52)
Age at diagnosis	
0-<2	13 (52)
2-18	12 (48)
> 18	0
mean	3y
Visceral involvement	3 (12)
Myofibromatosis status	
Multicentric	13 (52)
Solitary nodule	12 (48)
PDGFRB Mutants	
Single-hit	14 (56)
Multi-hits	11 (44)
Resurgence	0
Mortality	0
Protein domains	
Hotspots	17 (68)
Other	8 (31)

eFigure. Novel *PDGFRB* Mutations in Myofibroma Lesions Induce Constitutive Activation of PDGFRB and are Sensitive to Imatinib

We used a luciferase reporter that is sensitive to MAPK (A) or STAT (B) signaling pathways (see eMethod for details). The histogram represents the average of the ratio between luciferase and β-galactosidase activities of at least three independent experiments with standard error of the mean. Final concentration of imatinib was 500 nM. PDGFRB N666K, a positive control that was extensively studied before[7], was used as a reference to normalize the results, and all mutants were compared to the wild type using Student's t-test.



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