

56th ANNUAL DIAGNOSTIC SLIDE SESSION 2015

CASE 2015-9

American Association of Neuropathologists Annual Meeting - June 13th 2015

Phedias Diamandis, Brendan C. Dickson, Dennis Izukawa, Claire I. Coire

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PGY4, Neuropathology Resident
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Clinical Summary

ID: 71F

PMH & Family History:

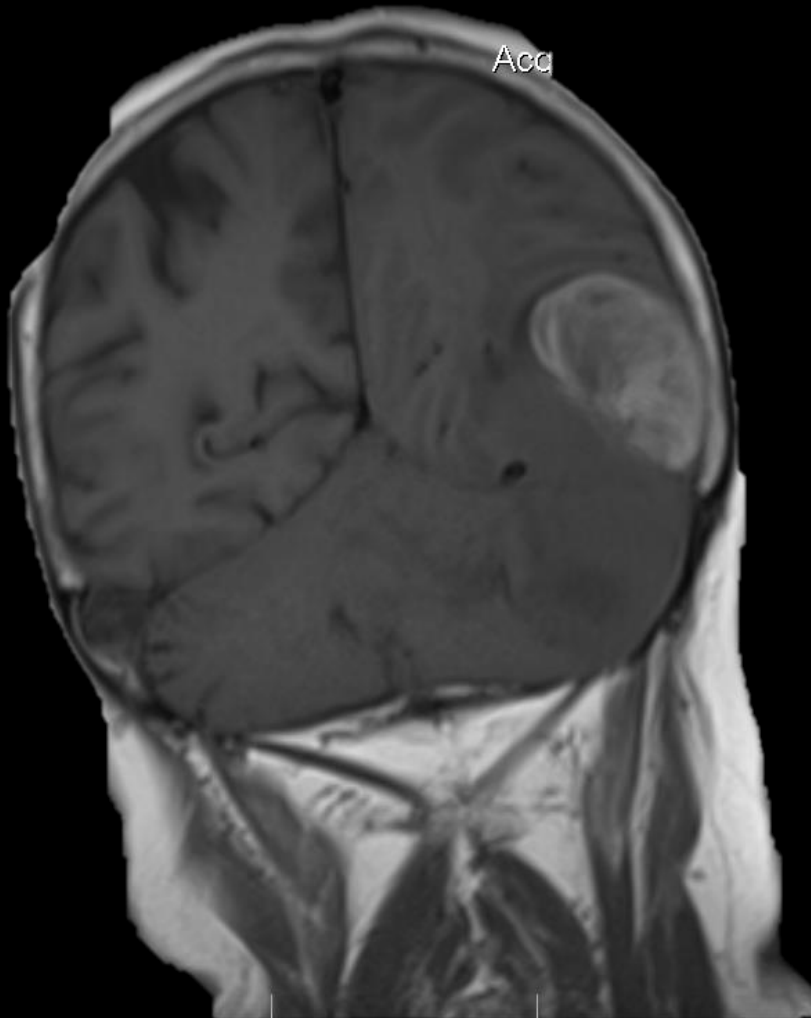
- Non-contributory

HPI:

- 6 months of declining speech function
- Sudden deterioration with worsening aphasia, right hemiparesis, unsteady gait

Imaging

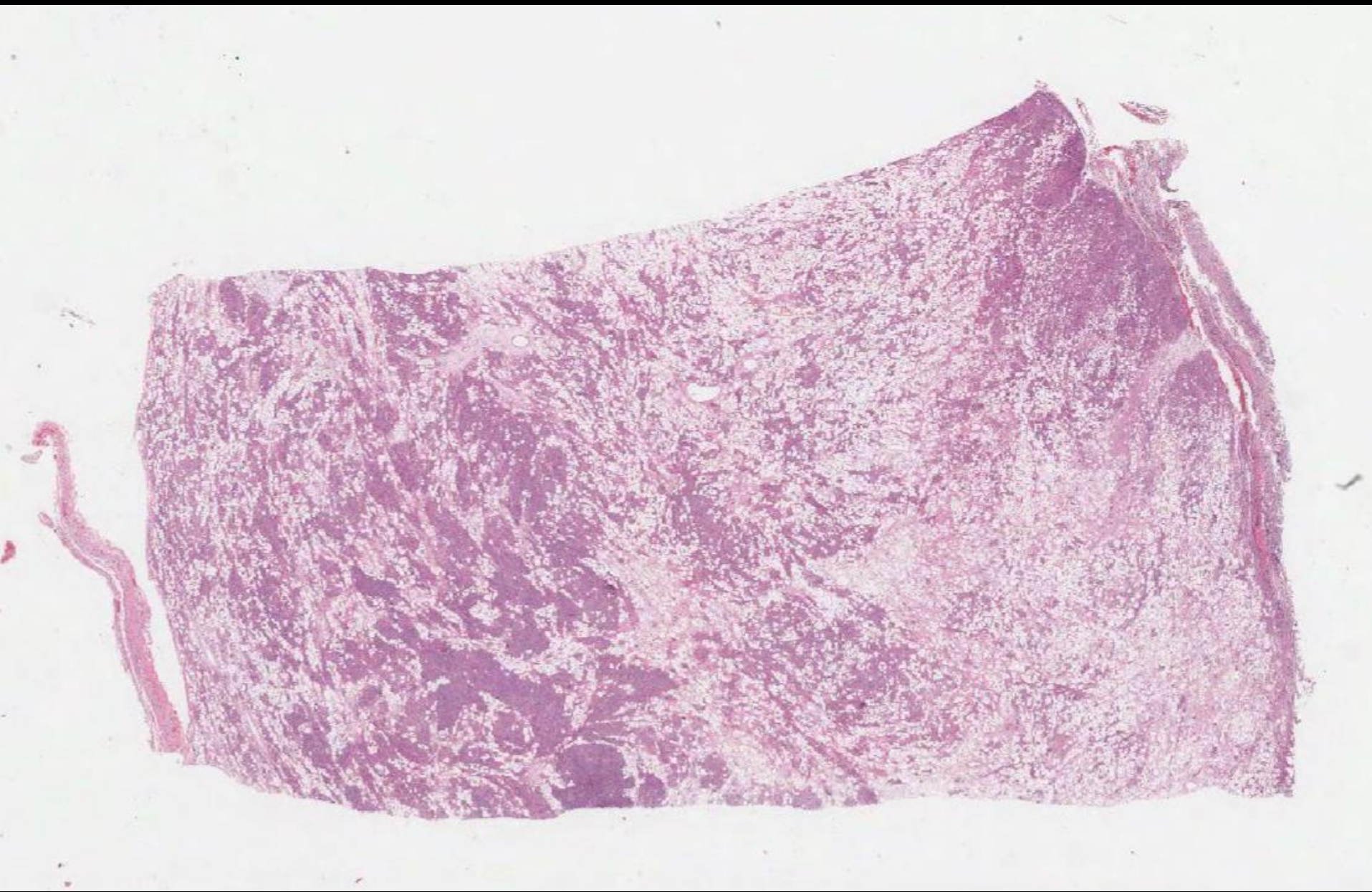
T1 without GAD

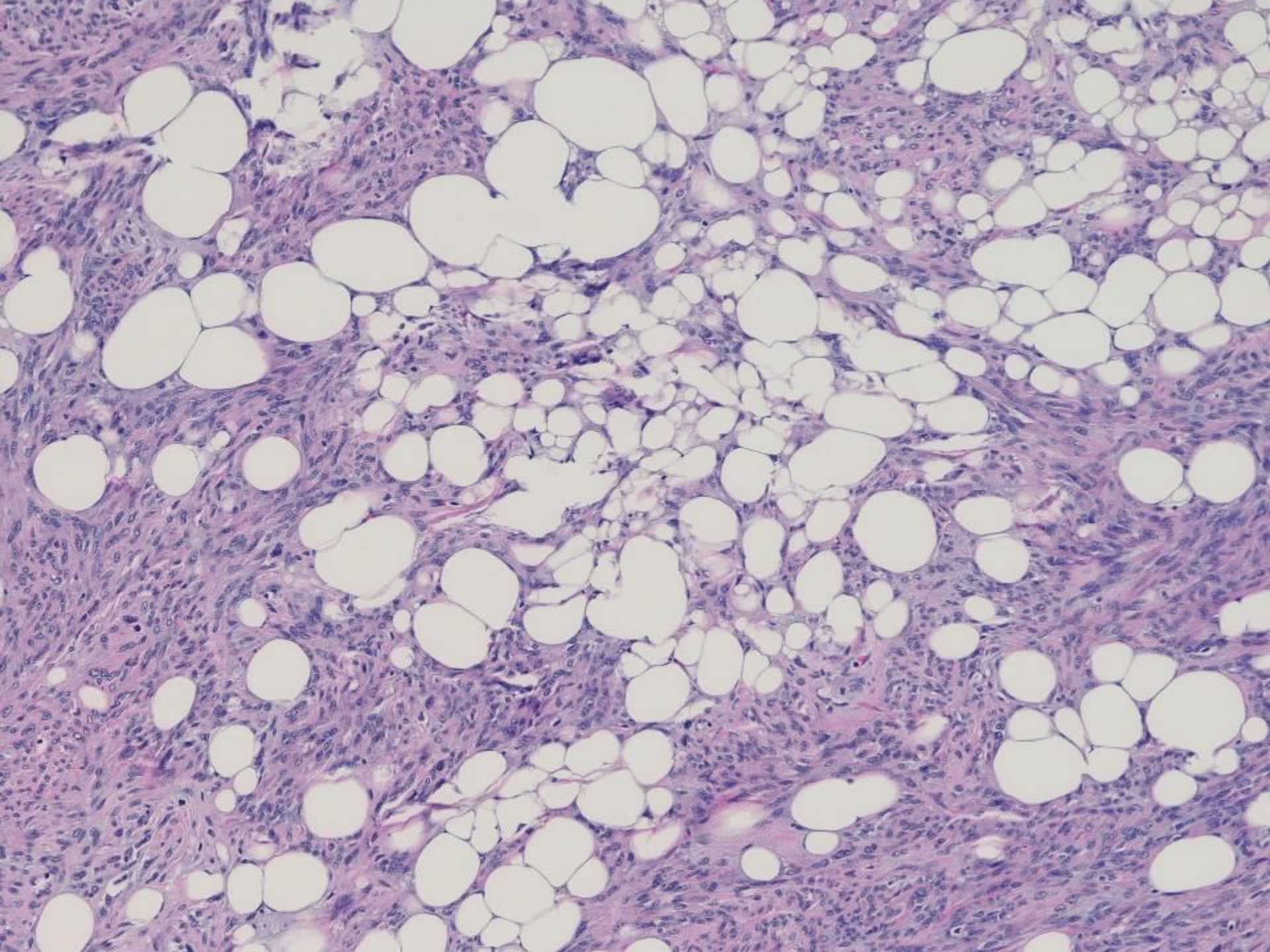


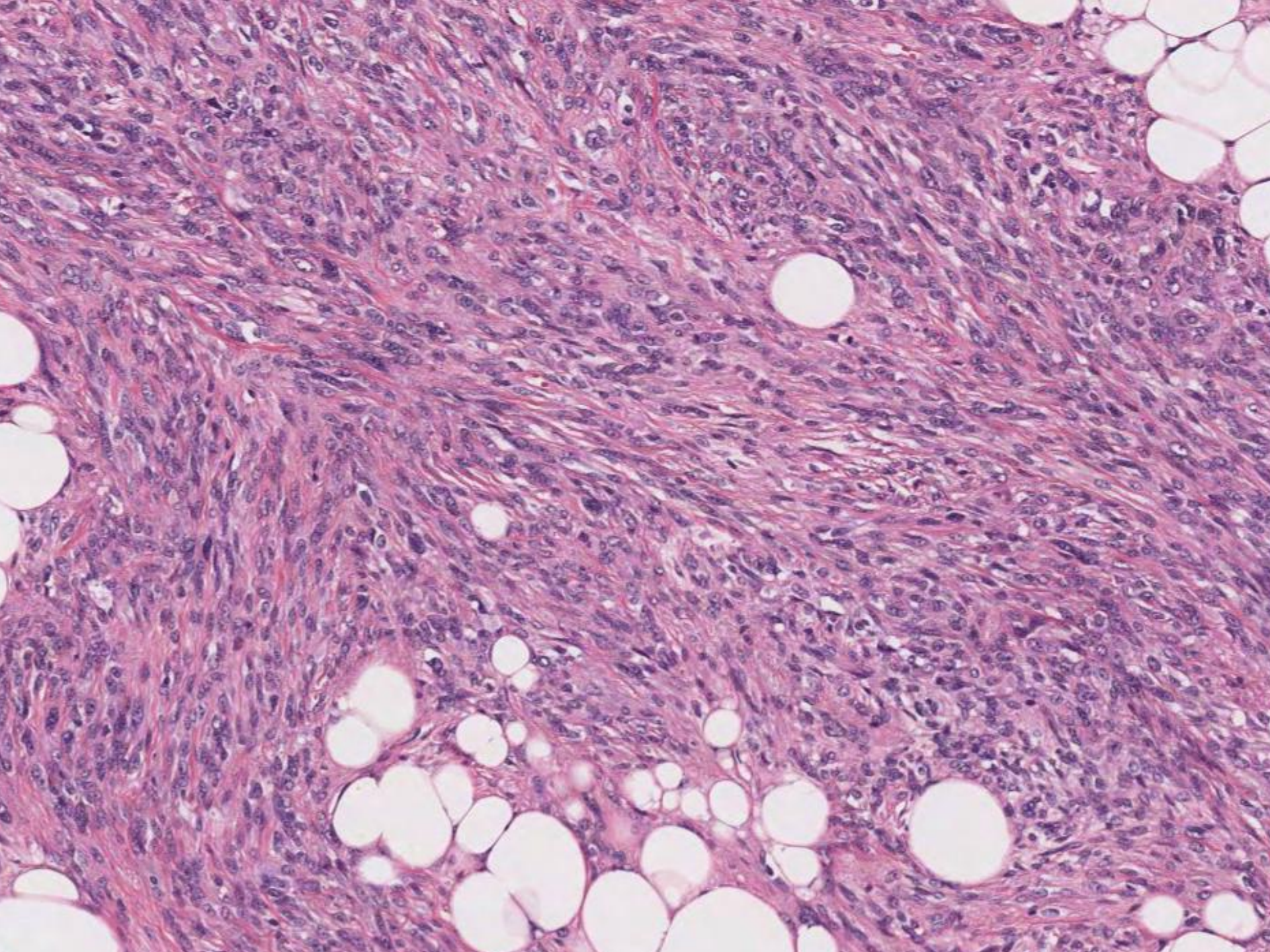
T1 with GAD

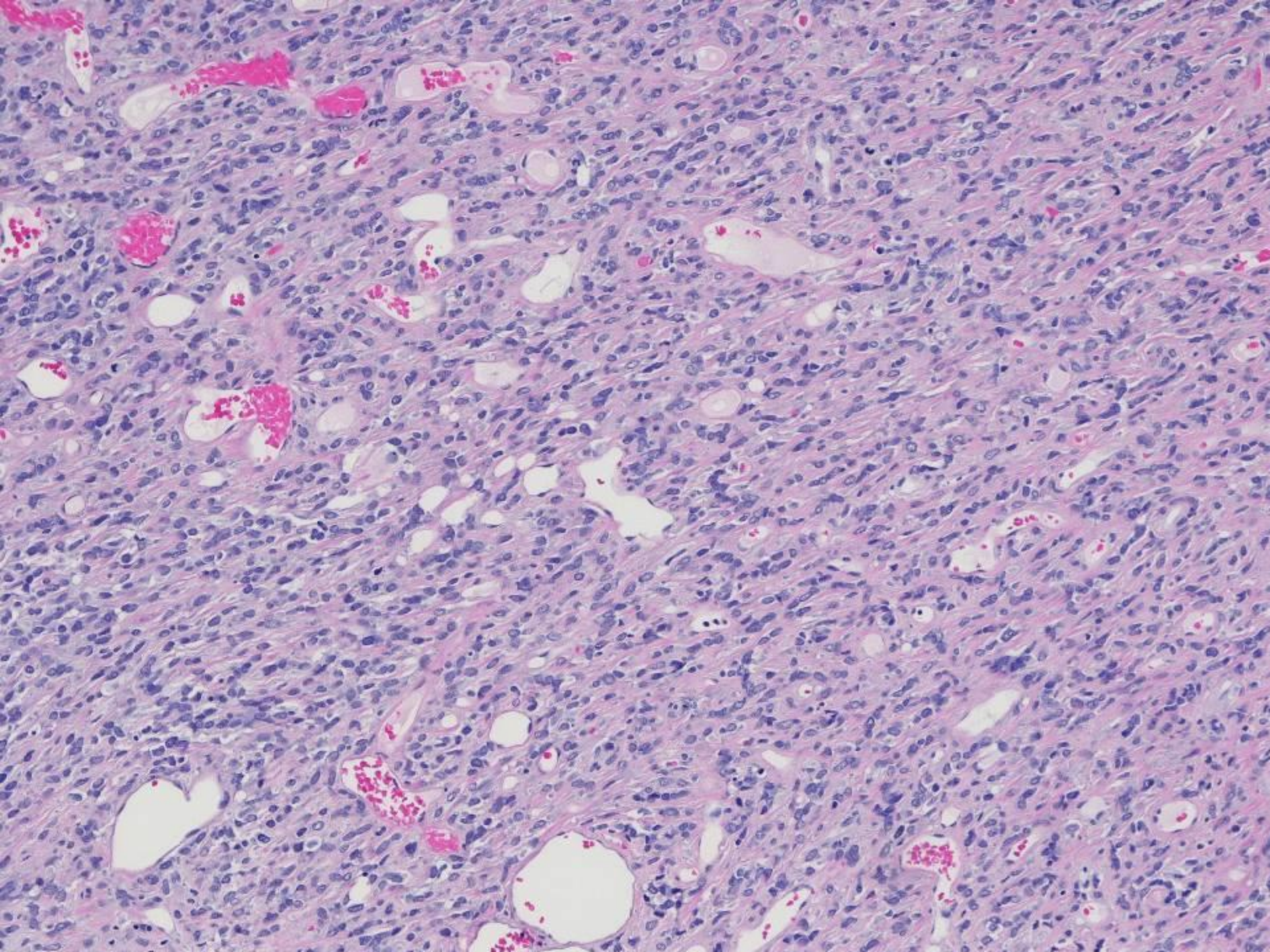


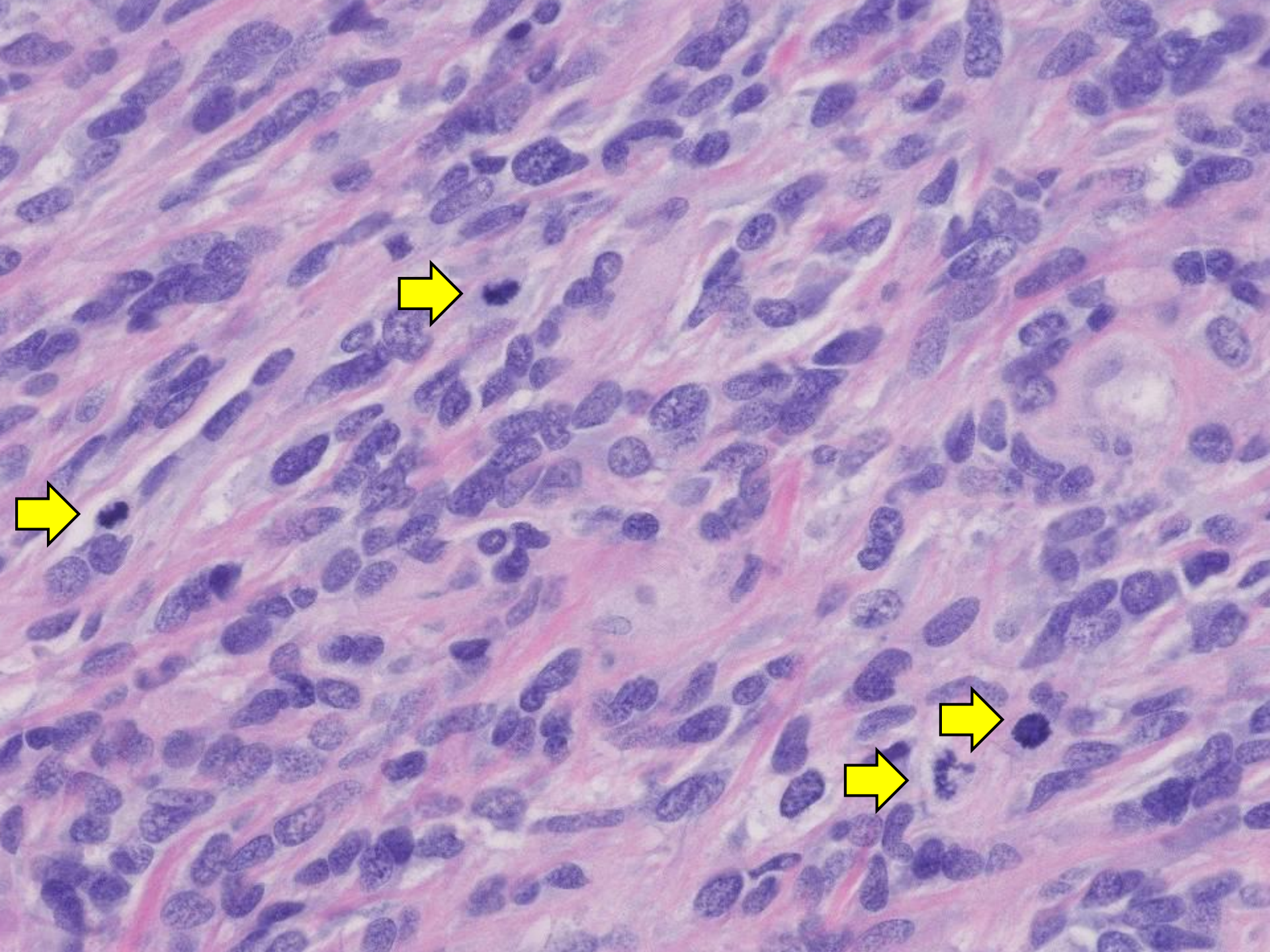
Submitted Slide



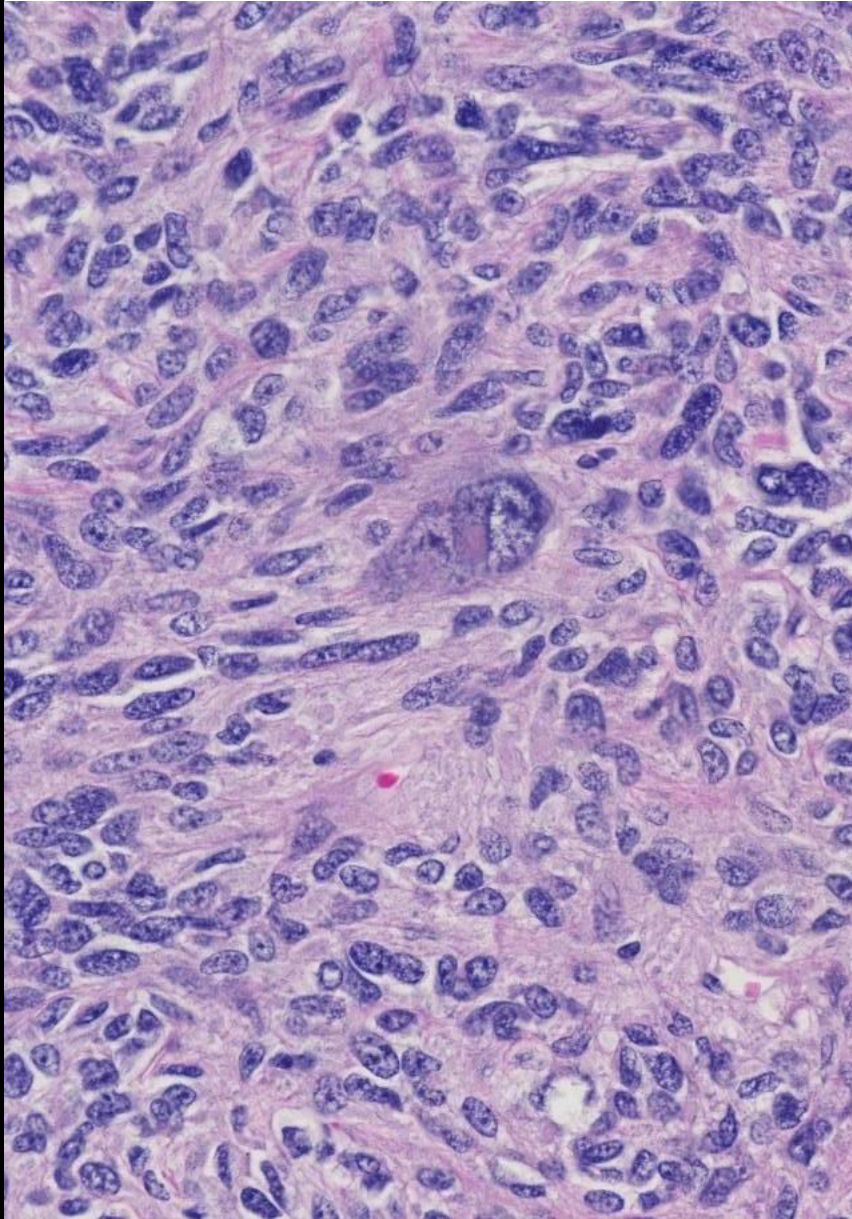




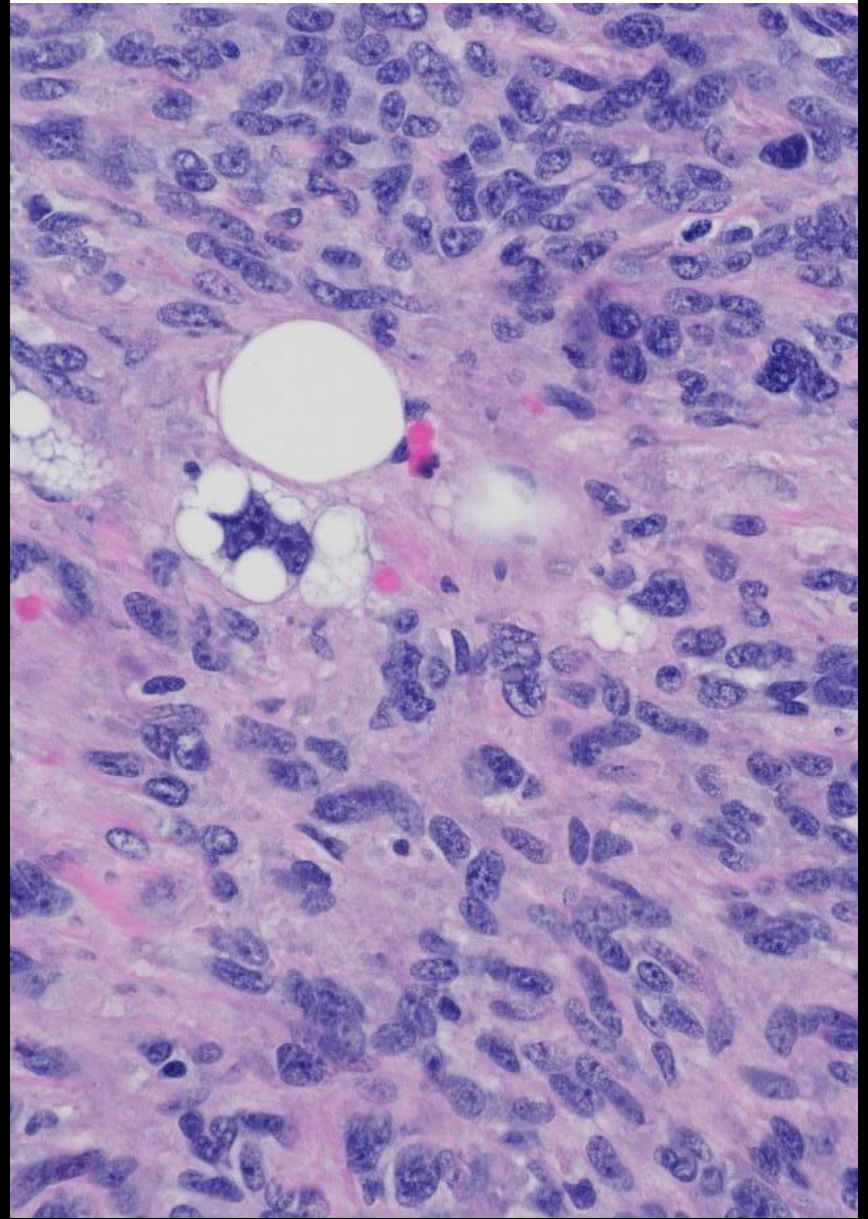




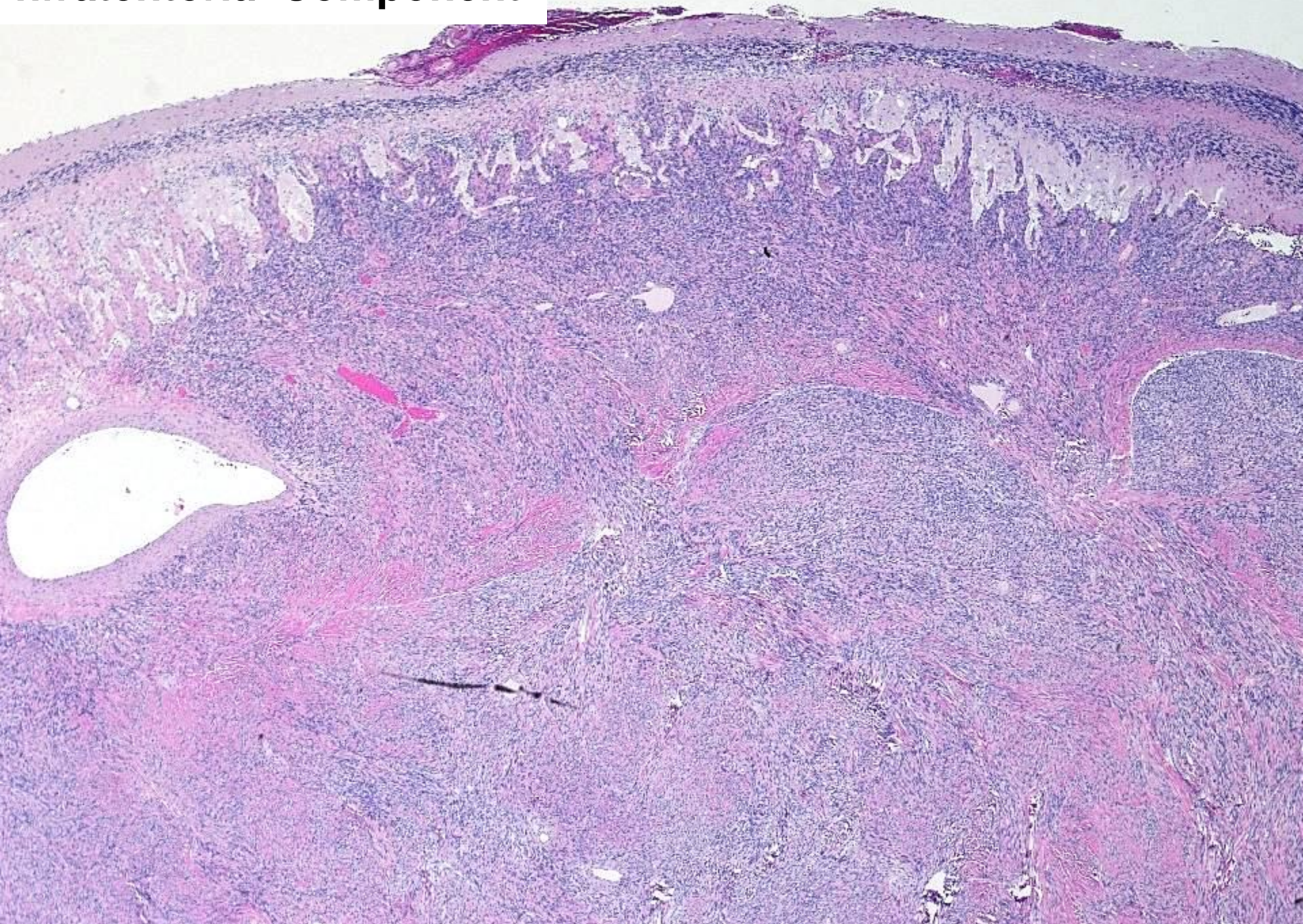
Marked nuclear atypia



Adiposidic nuclear scalloping



Infratentorial Component



Differential Diagnosis?

Additional Studies/Stains?

Differential Diagnosis

1. Malignant Fat-Forming Solitary Fibrous Tumor
2. Liposarcoma, dedifferentiated

Fat Forming SFTs

aka “lipomatous hemangiopericytoma”

- Nielsen et al (1995)
- Rare variant of SFT

Histology:

- Conventional SFT
- Variably prominent mature adipocytic component.

Prognosis:

- Generally follow benign indolent course

Malignant Fat Forming SFTs

Am J Surg Pathol • Volume 35, Number 8, August 2011

ORIGINAL ARTICLE

Malignant Fat-Forming Solitary Fibrous Tumor (so-called “Lipomatous Hemangiopericytoma”): Clinicopathologic Analysis of 14 Cases

Jen-Chieh Lee, MD† and Christopher D.M. Fletcher, MD, FRCPath†*

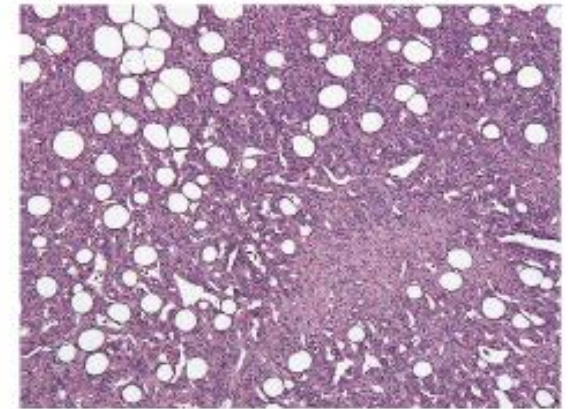
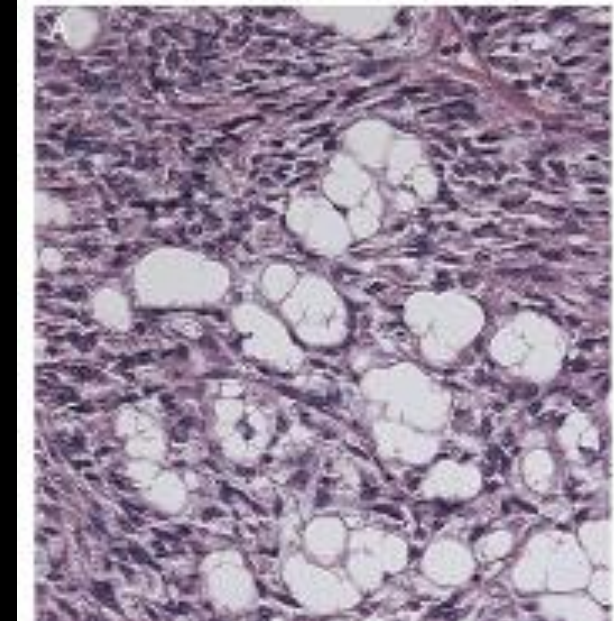


FIGURE 5. Mature adipocytes admixed with the SFT component.

Fat-forming SFTs with malignant histology:

- Very rare
- Histology:
 - Mitoses >4/10 high-power fields (HPF)
 - Hypercellularity (focal to diffuse)
 - Moderate/Severe atypia
 - Necrosis
 - Mature Adipose tissue +/- Lipoblast-like cells



Malignant Fat Forming SFTs

Immunohistochemistry:

- CD34
- CD99

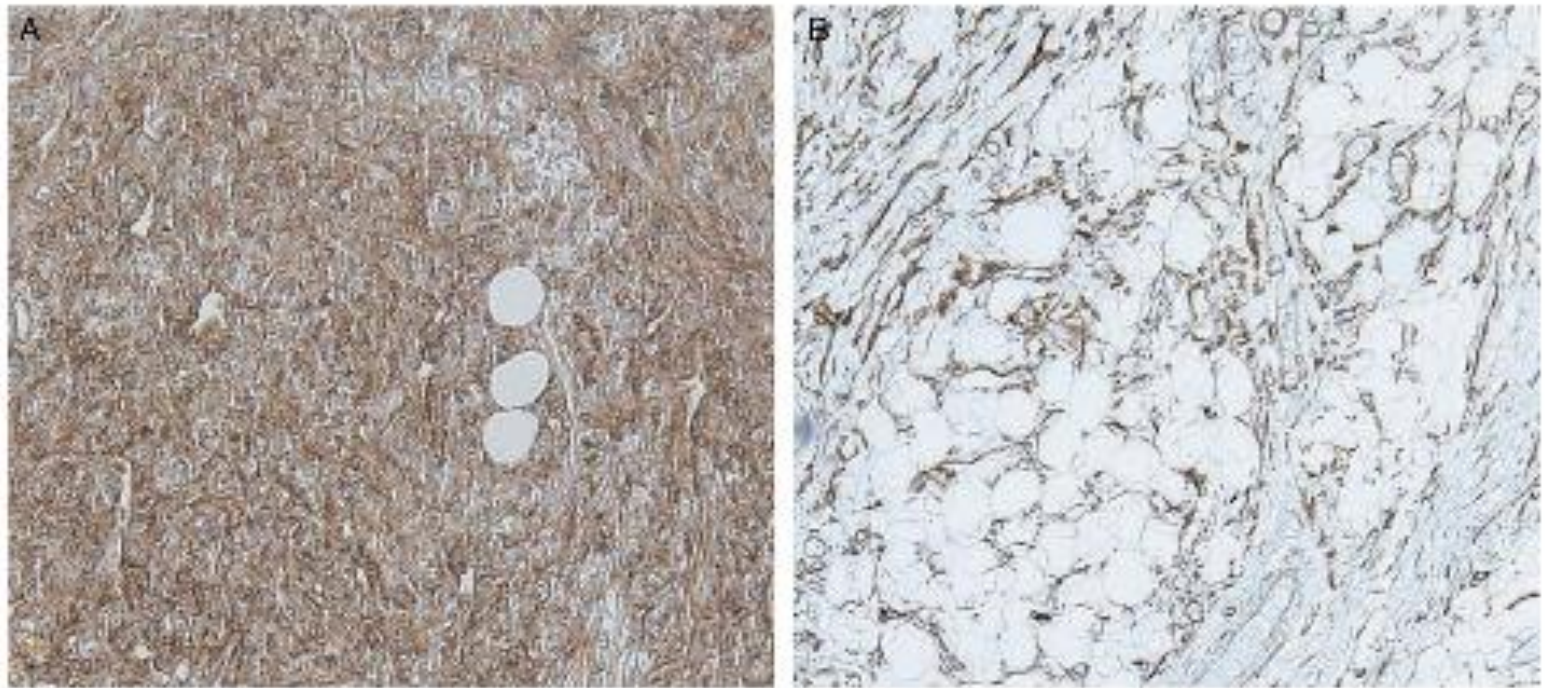
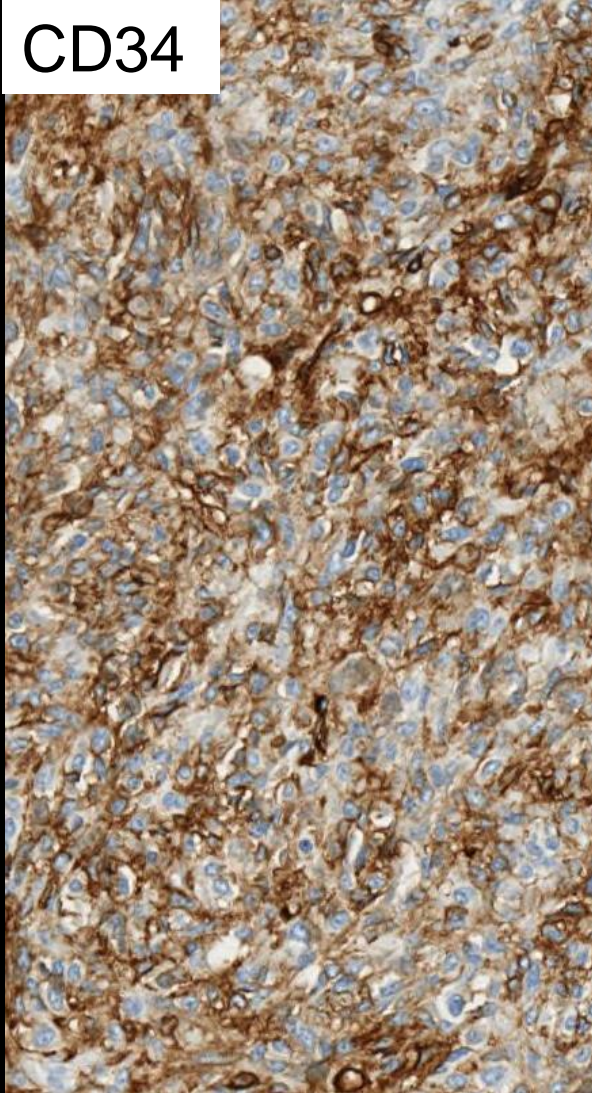


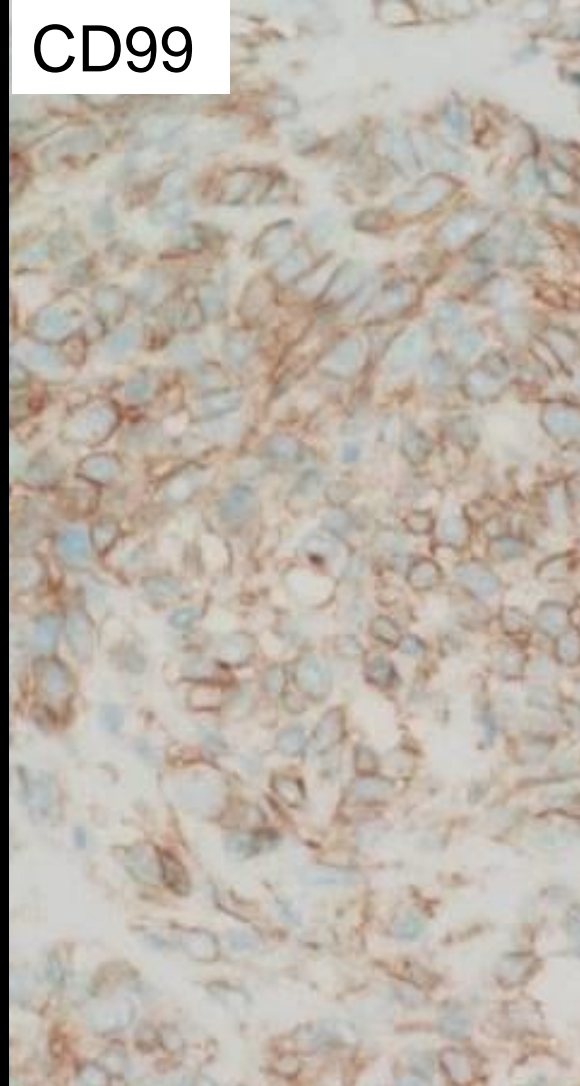
FIGURE 8. The neoplastic spindle cells usually stain for CD34 (A), including those in the ALT-like areas (B).

Case AANP 2015-9

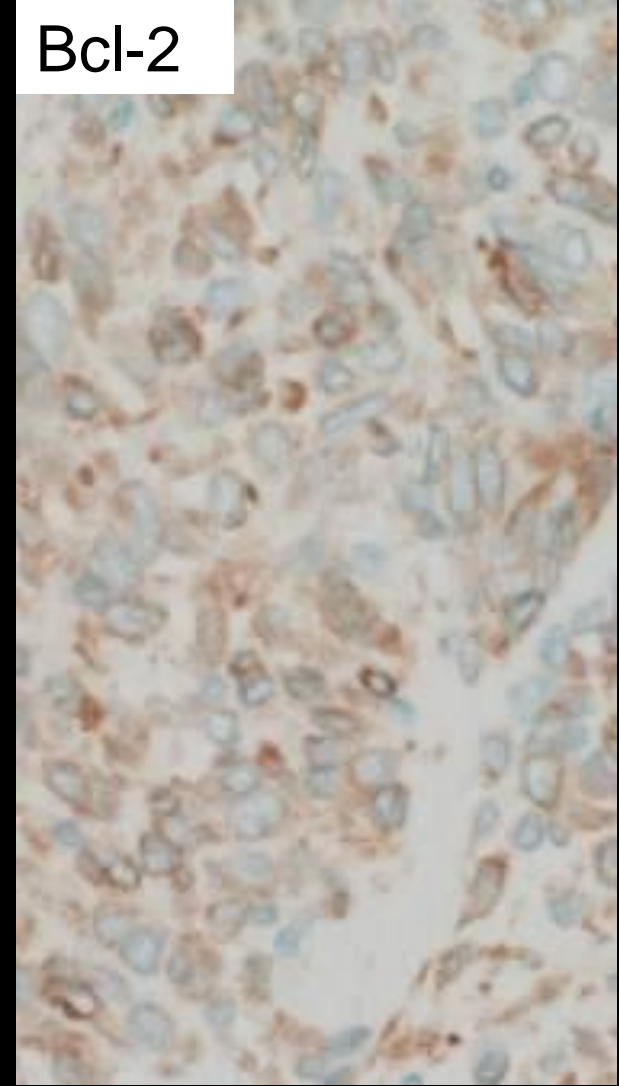
CD34



CD99



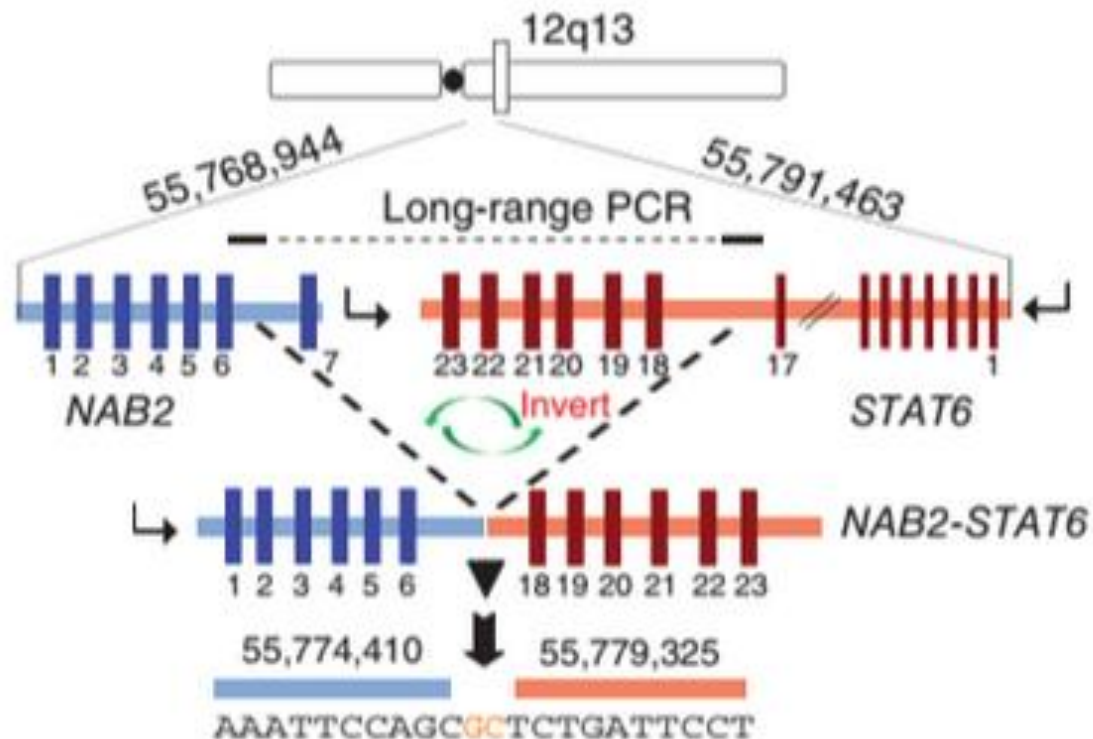
Bcl-2



Identification of recurrent *NAB2-STAT6* gene fusions in solitary fibrous tumor by integrative sequencing

Dan R Robinson^{1,2,12}, Yi-Mi Wu^{1,2,12}, Shanker Kalyana-Sundaram¹⁻³, Xuhong Cao^{1,4}, Robert J Lonigro^{1,5}, Yun-Shao Sung⁶, Chun-Liang Chen⁶, Lei Zhang⁶, Rui Wang^{1,2}, Fengyun Su^{1,2}, Matthew K Iyer^{1,7}, Sameek Roychowdhury^{1,8}, Javed Siddiqui^{1,2}, Kenneth J Pienta^{1,5,8,9}, Lakshmi P Kunju^{1,2}, Moshe Talpaz^{5,8}, Juan Miguel Mosquera¹⁰, Samuel Singer¹¹, Scott M Schuetz^{5,8}, Cristina R Antonescu⁶ & Arul M Chinnaiyan^{1,2,4,5,7,9}

NATURE GENETICS VOLUME 45 | NUMBER 2 | FEBRUARY 2013



Identification of recurrent *NAB2-STAT6* gene fusions in solitary fibrous tumor by integrative sequencing

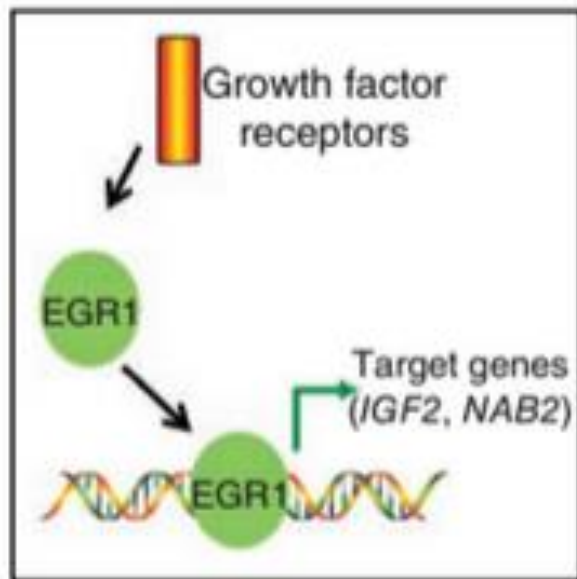
Dan R Robinson^{1,2,12}, Yi-Mi Wu^{1,2,12}, Shanker Kalyana-Sundaram¹⁻³, Xuhong Cao^{1,4}, Robert J Lonigro^{1,5}, Yun-Shao Sung⁶, Chun-Liang Chen⁶, Lei Zhang⁶, Rui Wang^{1,2}, Fengyun Su^{1,2}, Matthew K Iyer^{1,7}, Sameek Roychowdhury^{1,8}, Javed Siddiqui^{1,2}, Kenneth J Pienta^{1,5,8,9}, Lakshmi P Kunju^{1,2}, Moshe Talpaz^{5,8}, Juan Miguel Mosquera¹⁰, Samuel Singer¹¹, Scott M Schuetze^{5,8}, Cristina R Antonescu⁶ & Arul M Chinnaiyan^{1,2,4,5,7,9}

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NAB2



Normal cells



Growth response

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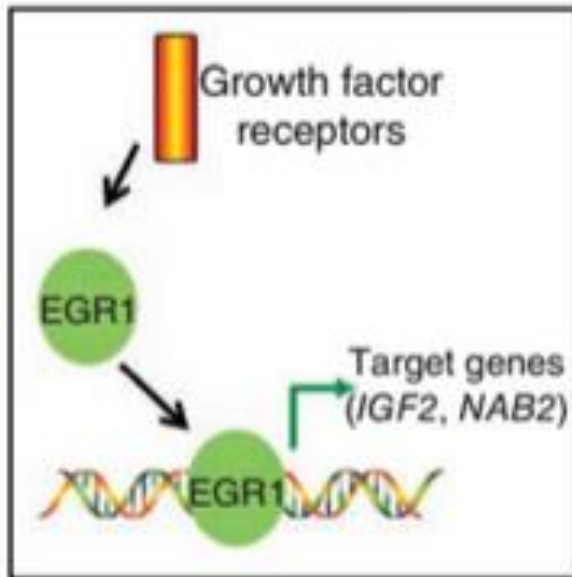
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NAB2



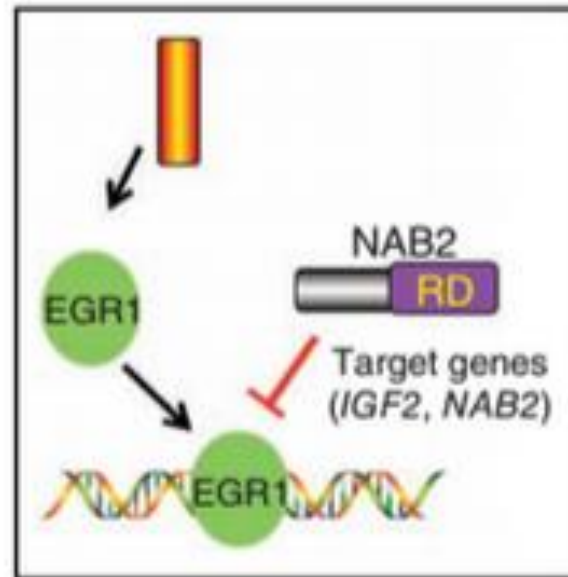
A schematic diagram of the NAB2 protein structure. It is represented as a horizontal bar with four colored segments: a yellow segment labeled 'EBD' (residues 34-115), a grey segment (residues 115-252), a yellow segment labeled 'NCD2' (residues 252-352), and an orange segment labeled 'RD' (residues 352-525). The residue numbers 34, 115, 252, 352, and 525 are positioned above the corresponding segments.

Normal cells



Growth response

Normal cells

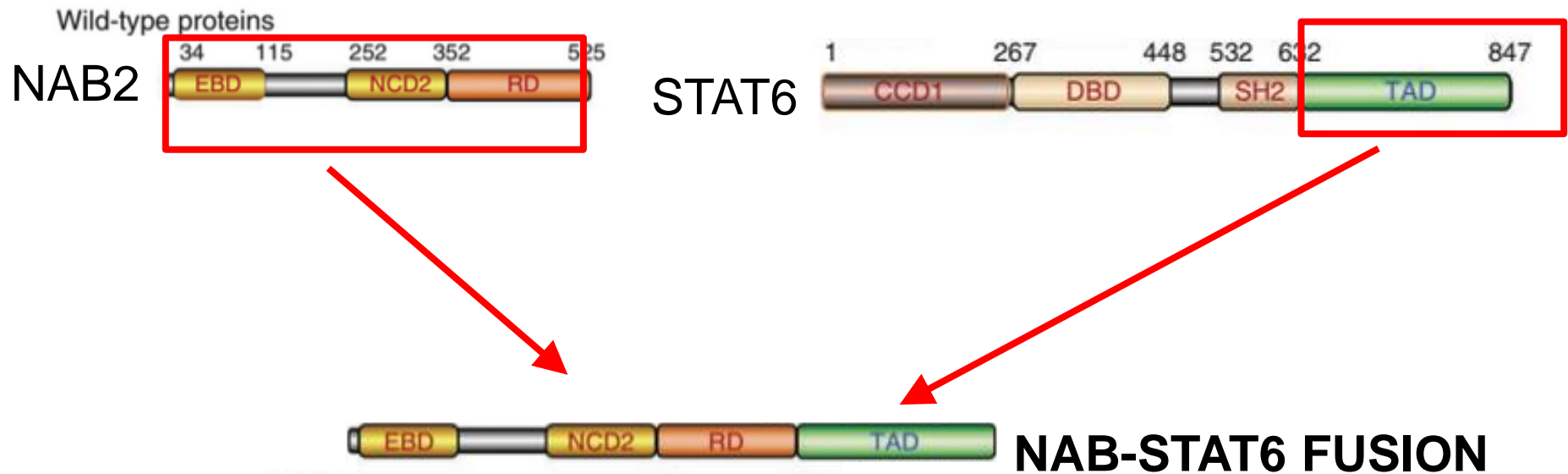


Feedback inhibition

Identification of recurrent *NAB2-STAT6* gene fusions in solitary fibrous tumor by integrative sequencing

Dan R Robinson^{1,2,12}, Yi-Mi Wu^{1,2,12}, Shanker Kalyana-Sundaram¹⁻³, Xuhong Cao^{1,4}, Robert J Lonigro^{1,5}, Yun-Shao Sung⁶, Chun-Liang Chen⁶, Lei Zhang⁶, Rui Wang^{1,2}, Fengyun Su^{1,2}, Matthew K Iyer^{1,7}, Sameek Roychowdhury^{1,8}, Javed Siddiqui^{1,2}, Kenneth J Pienta^{1,5,8,9}, Lakshmi P Kunju^{1,2}, Moshe Talpaz^{5,8}, Juan Miguel Mosquera¹⁰, Samuel Singer¹¹, Scott M Schuetze^{5,8}, Cristina R Antonescu⁶ & Arul M Chinnaiyan^{1,2,4,5,7,9}

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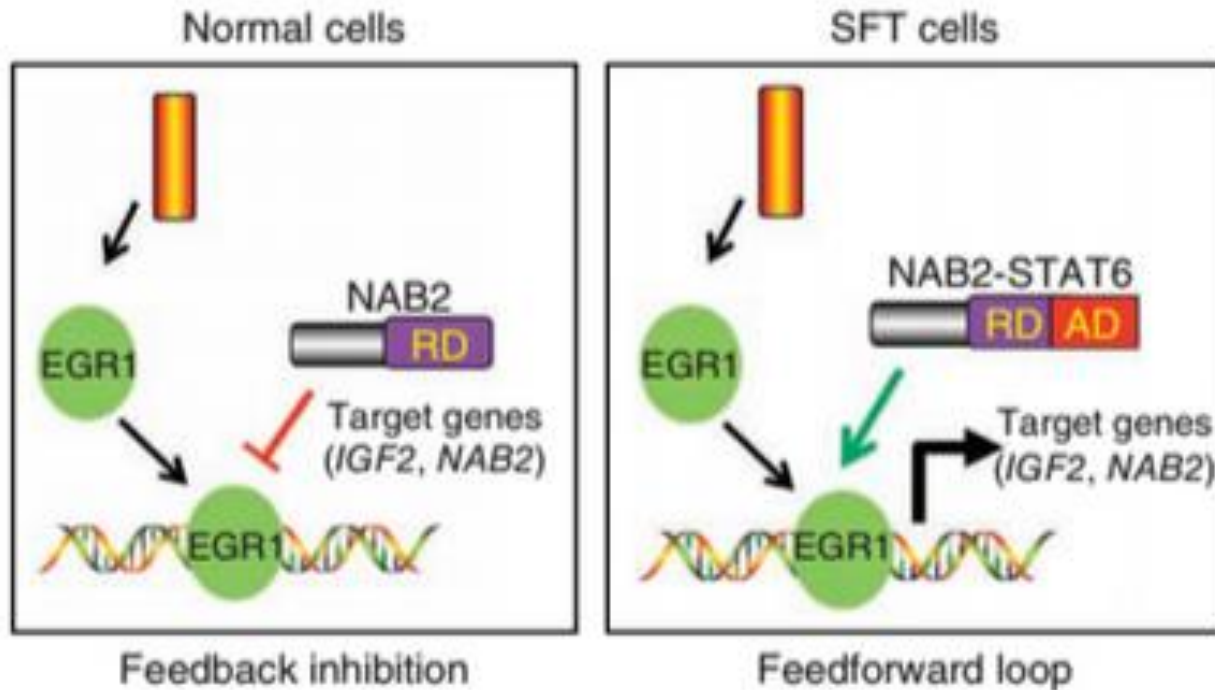
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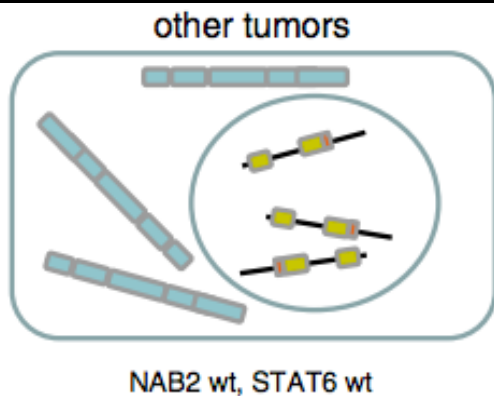


NAB-STAT6 FUSION

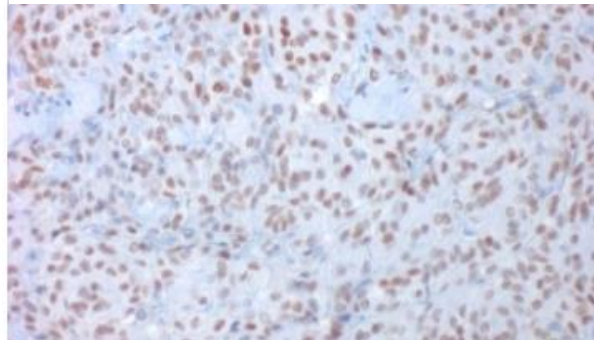


Meningeal hemangiopericytoma and solitary fibrous tumors carry the *NAB2-STAT6* fusion and can be diagnosed by nuclear expression of STAT6 protein

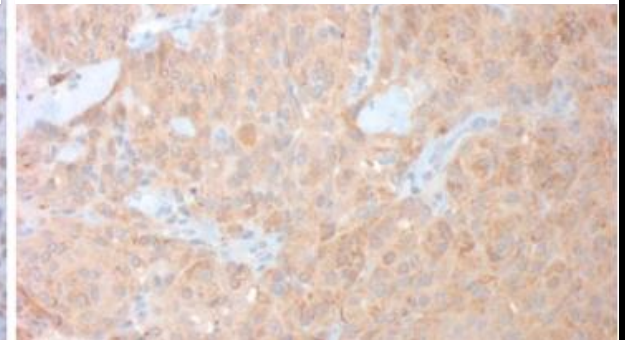
Leonille Schweizer · Christian Koelsche · Felix Sahm · Rosario M. Piro · David Capper · David E. Reuss · Stefan Pusch · Antje Habel · Jochen Meyer · Tanja Göck · David T. W. Jones · Christian Mawrin · Jens Schittenhelm · Albert Becker · Stephanie Heim · Matthias Simon · Christel Herold-Mende · Gunhild Meckersheimer · Werner Paulus · Rainer König · Otmar D. Wiestler · Stefan M. Pfister · Andreas von Deimling



Meningioma - NAB2



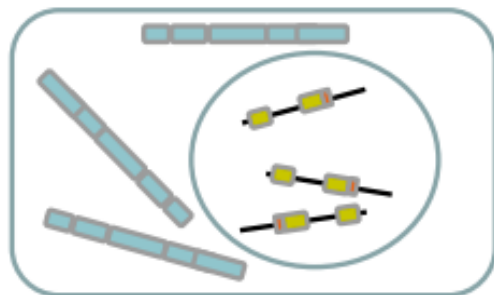
Meningioma - STAT6



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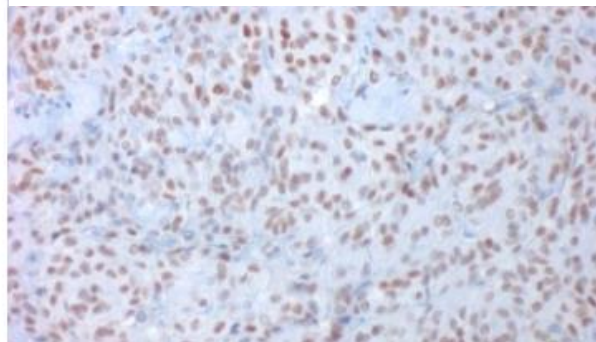
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other tumors

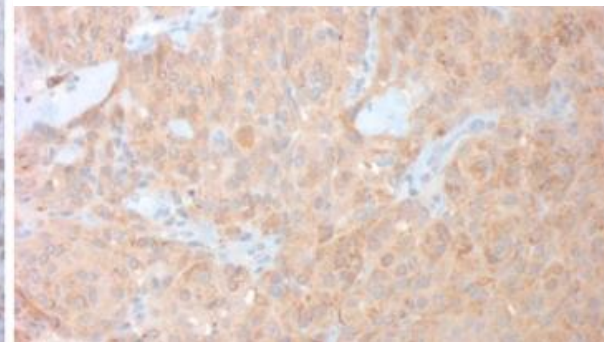


NAB2 wt, STAT6 wt

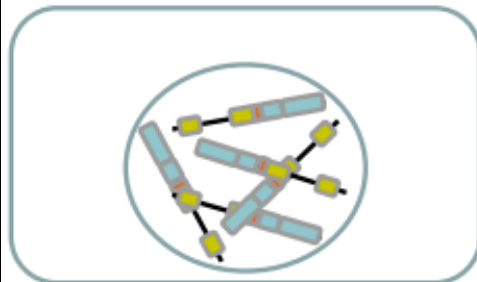
Meningioma - NAB2



Meningioma - STAT6

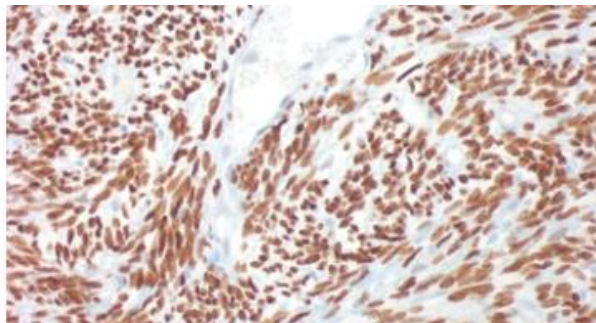


HPC/SFT

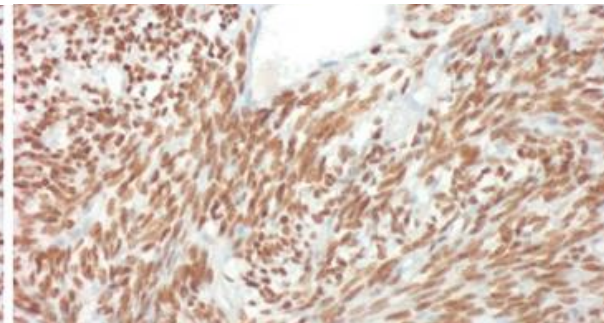


NAB2-STAT6 fusion

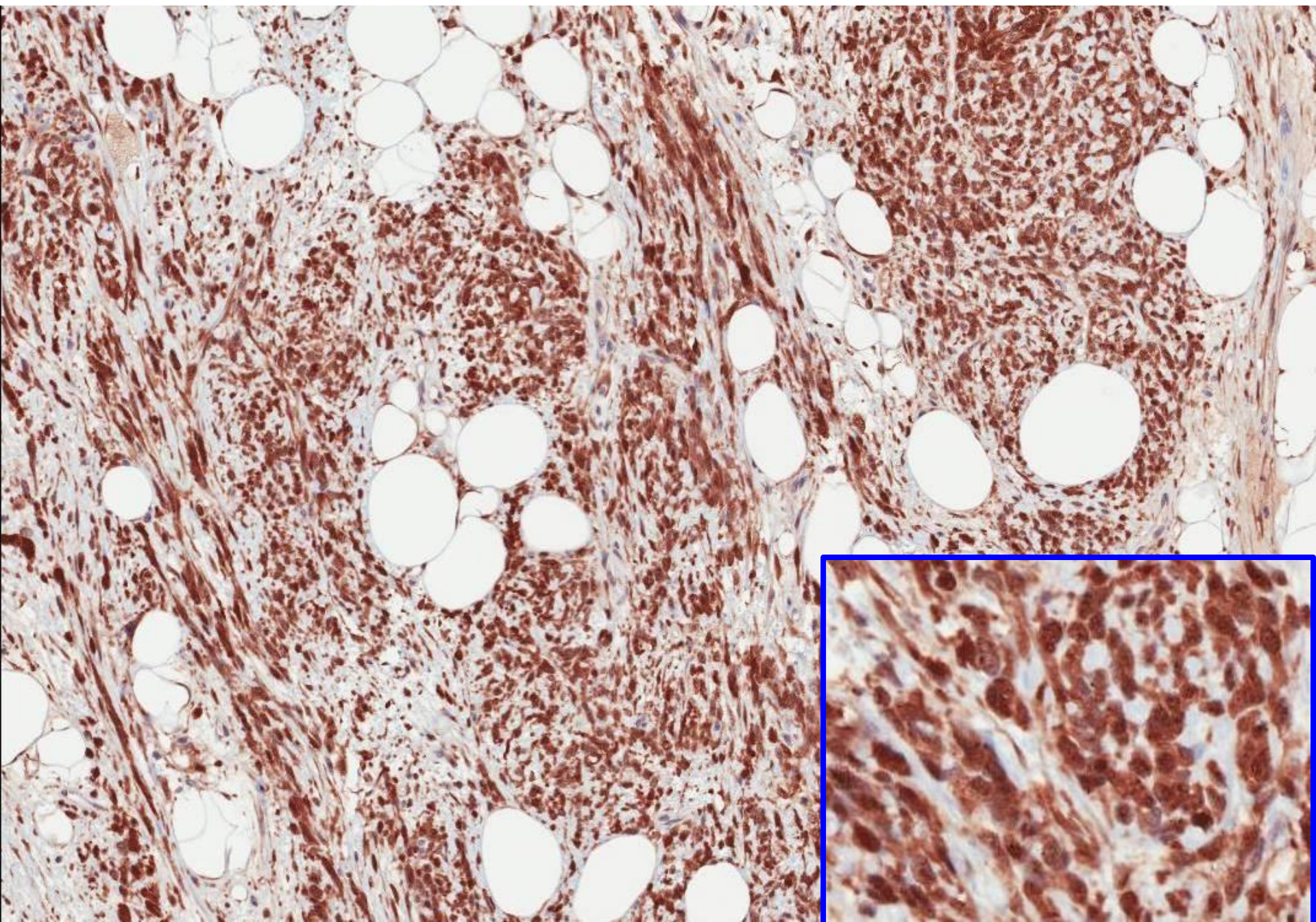
SFT-NAB2



SFT-STAT6



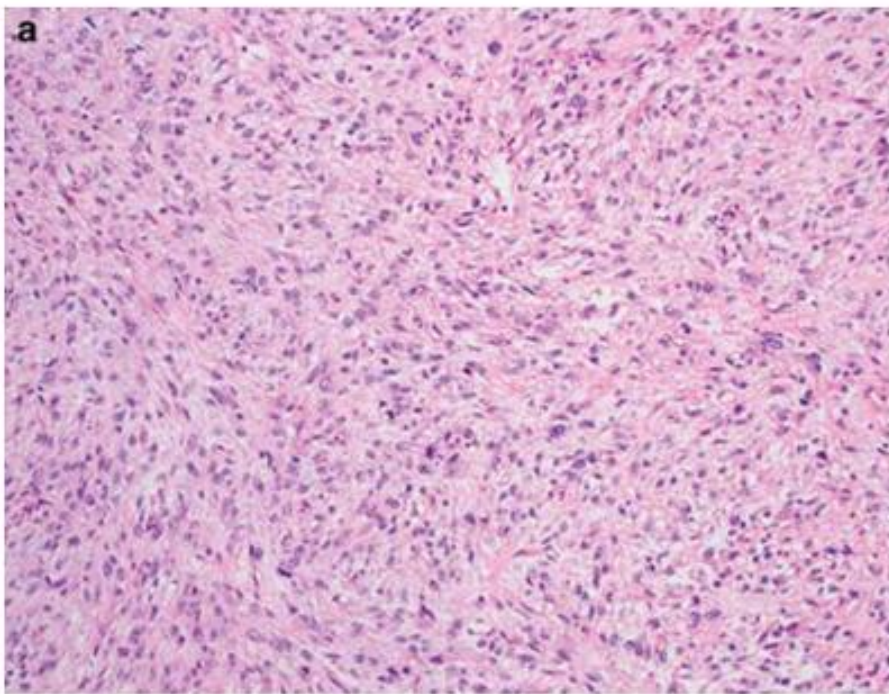
Case AANP 2015-9 - STAT6



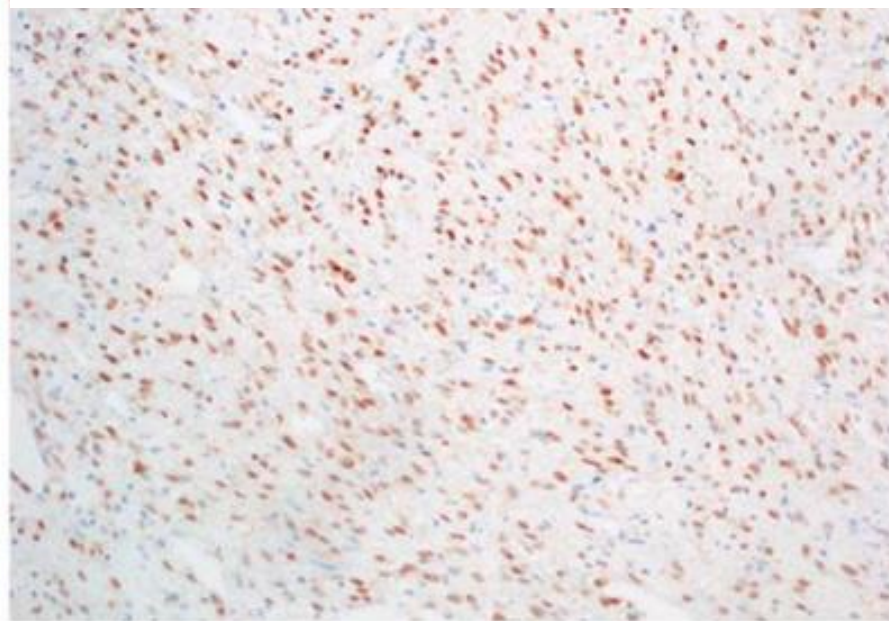
STAT6 is amplified in a subset of dedifferentiated liposarcoma

Leona A Doyle, Derrick Tao and Adrián Mariño-Enríquez

Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA



STAT6



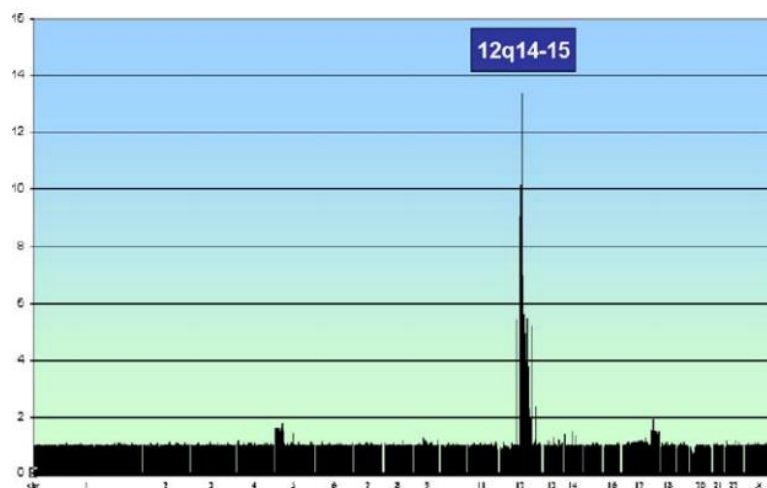
Well-differentiated and dedifferentiated liposarcomas

Jean-Michel Coindre • Florence Pédeutour •
Alain Aurias

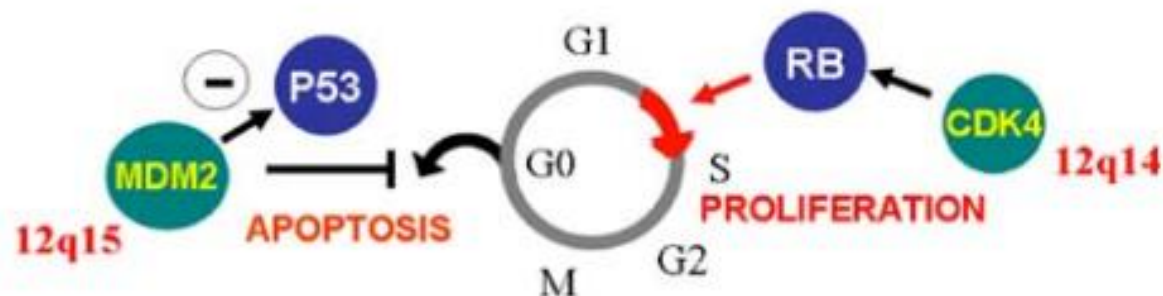
Virchows Arch (2010) 456:167–179

169

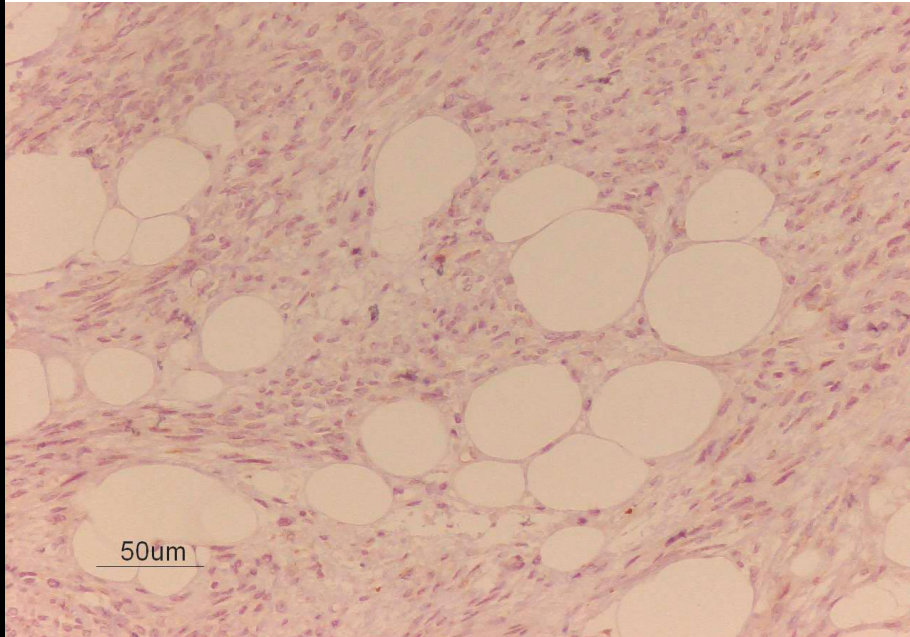
Fig. 2 Array CGH in an ALT-WDLPS showing an amplification of the 12q14–15 involving *MDM2* and *CDK4* genes



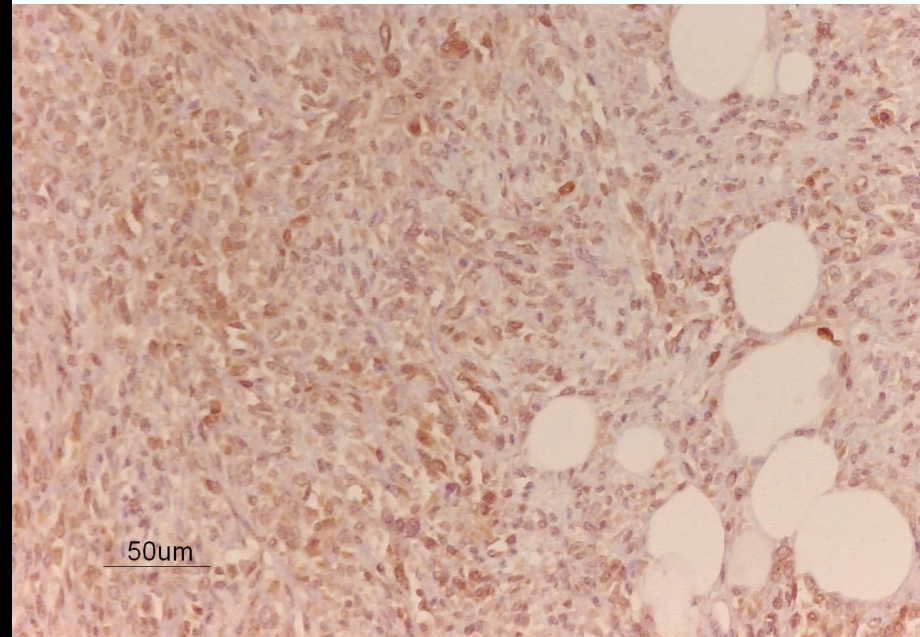
MDM2 and CDK4 in the cell cycle



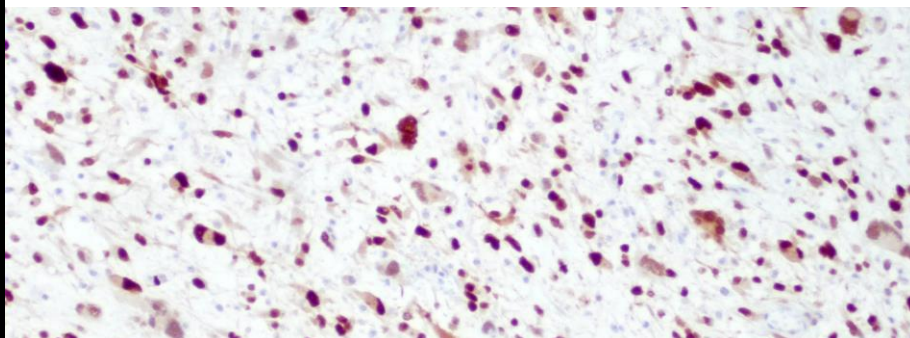
MDM2 - Case AANP 2015-9



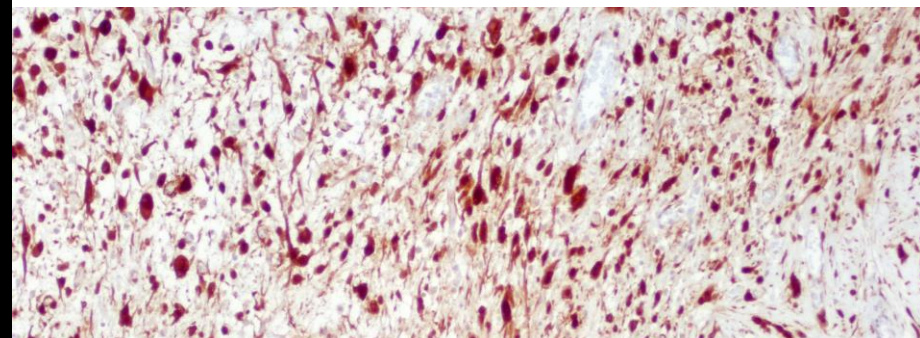
CDK4 - Case AANP 2015-9



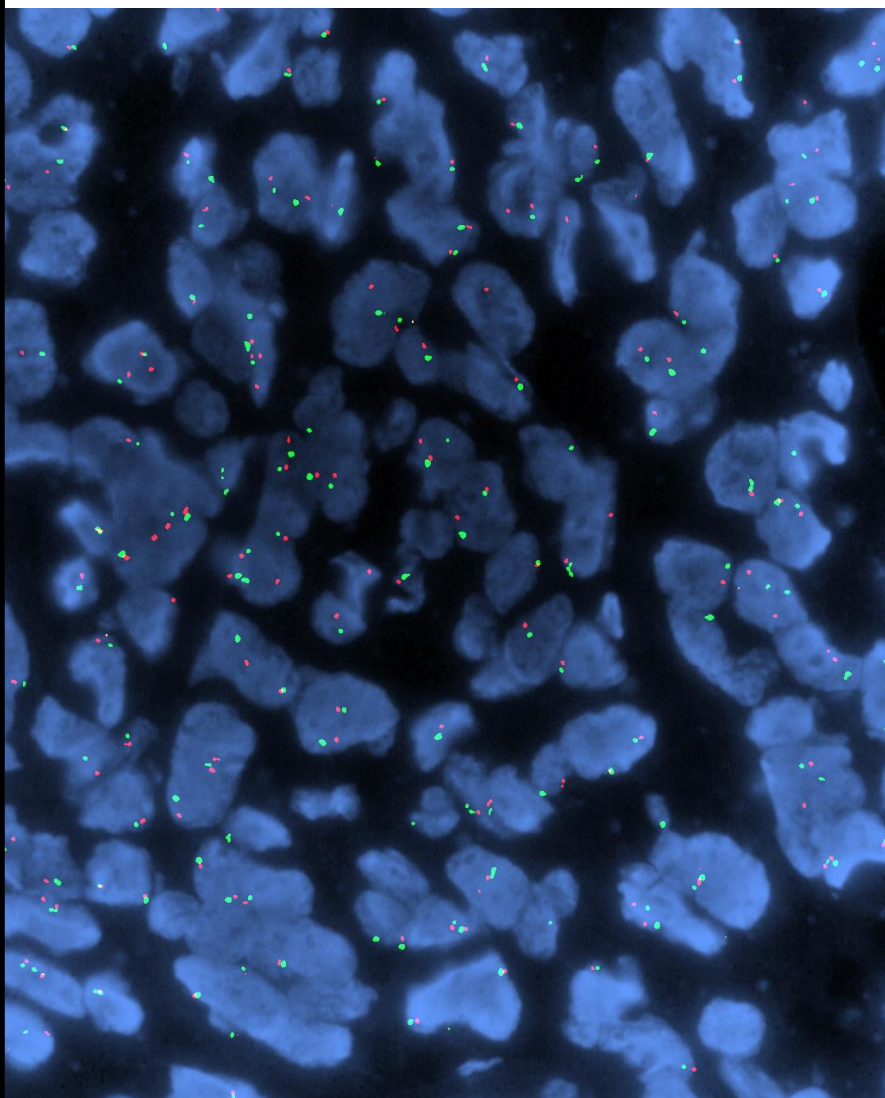
MDM2 - Positive



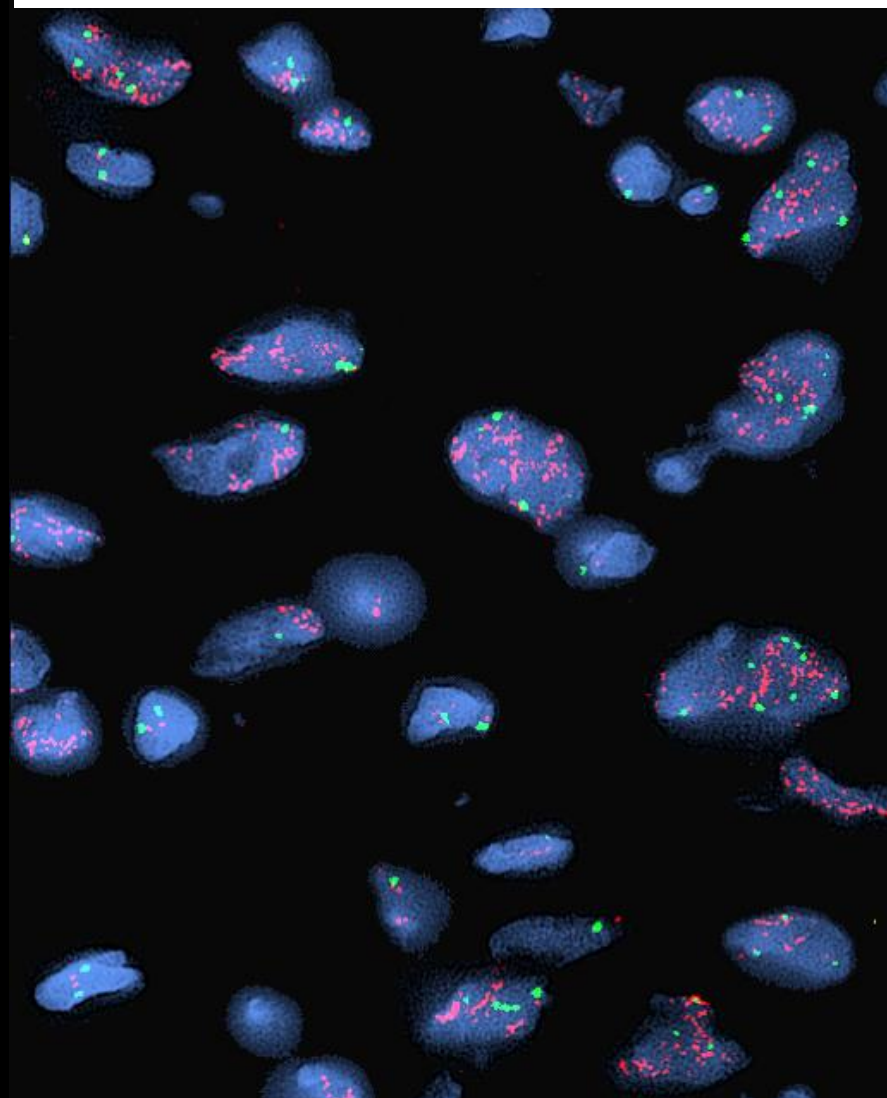
CDK4 - Positive



MDM2 (FISH) - Case AANP 2015-9



MDM2 (FISH) - Positive Control

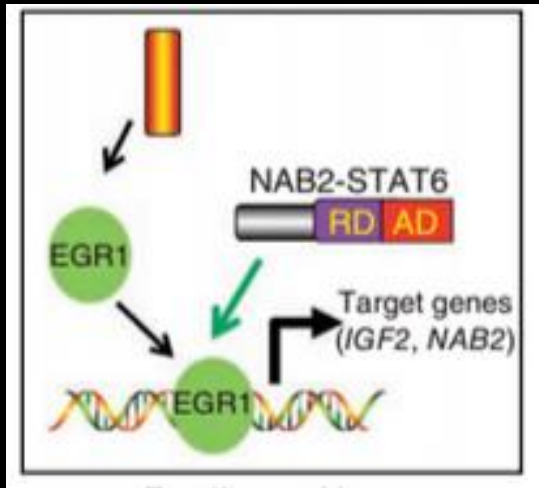


Diagnosis

Malignant Fat-Forming Solitary Fibrous
Tumor

Implications

SFT

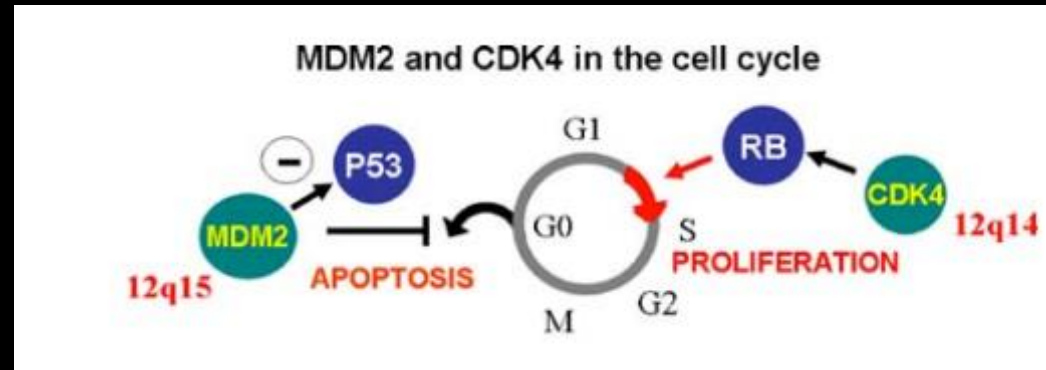


Sunitinib Malate and Figitumumab in Solitary Fibrous Tumor: Patterns and Molecular Bases of Tumor Response

Silvia Stacchiotti¹, Tiziana Negri², Elena Palassini¹, Elena Conca², Alessandro Gronchi³, Carlo Morosi⁴, Antonella Messina⁴, Ugo Pastorino³, Marco A. Pierotti⁵, Paolo G. Casali¹, and Silvana Pilotti²

Mol Cancer Ther; 9(5) May 2010

Liposarcoma



Effect of the MDM2 antagonist RG7112 on the P53 pathway in patients with *MDM2*-amplified, well-differentiated or dedifferentiated liposarcoma: an exploratory proof-of-mechanism study

Isabelle Ray-Coquard, Jean-Yves Blay, Antoine Italiano, Axel Le Cesne, Nicolas Penel, Jianguo Zhi, Florian Heil, Ruediger Rueger, Bradford Graves, Meichun Ding, David Geho, Steven A Middleton, Lyubomir T Vassilev, Gwen L Nichols, Binh Nguyen Bui

Lancet Oncol 2012; 13: 1133-40

Thank you

