

# 細胞・症例・診断・分類 病理セルフポートレート



*Shigeo Nakamura  
Nagoya University Hospital, Japan*

# 今日のお話

- 1) プロファイル
- 2) 細胞
- 3) 症例
- 4) 診断
- 5) 分類

メッセージ： 人との出会い、その重要性について

# 名古屋大学医学部附属病院 検査部・検査医学講座



牛島 宥教授  
初代専任部長  
昭和48年就任  
福岡県出身  
昭和19年卒



竹内 純教授  
初代検査医学講座教授  
昭和60年就任  
秋田県出身  
昭和29年卒



中島伸夫教授  
第二代検査医学講座教授  
平成 4年就任  
愛知県出身  
昭和40年卒





Shigeo Nakamura

中村栄男 Shigeo Nakamura  
名古屋大学大学院臓器病態診断学教授  
名古屋大学医学部附属病院病理部部长

### 職歴・研究歴

1979-1981: 内科研修医 社会保険中京病院

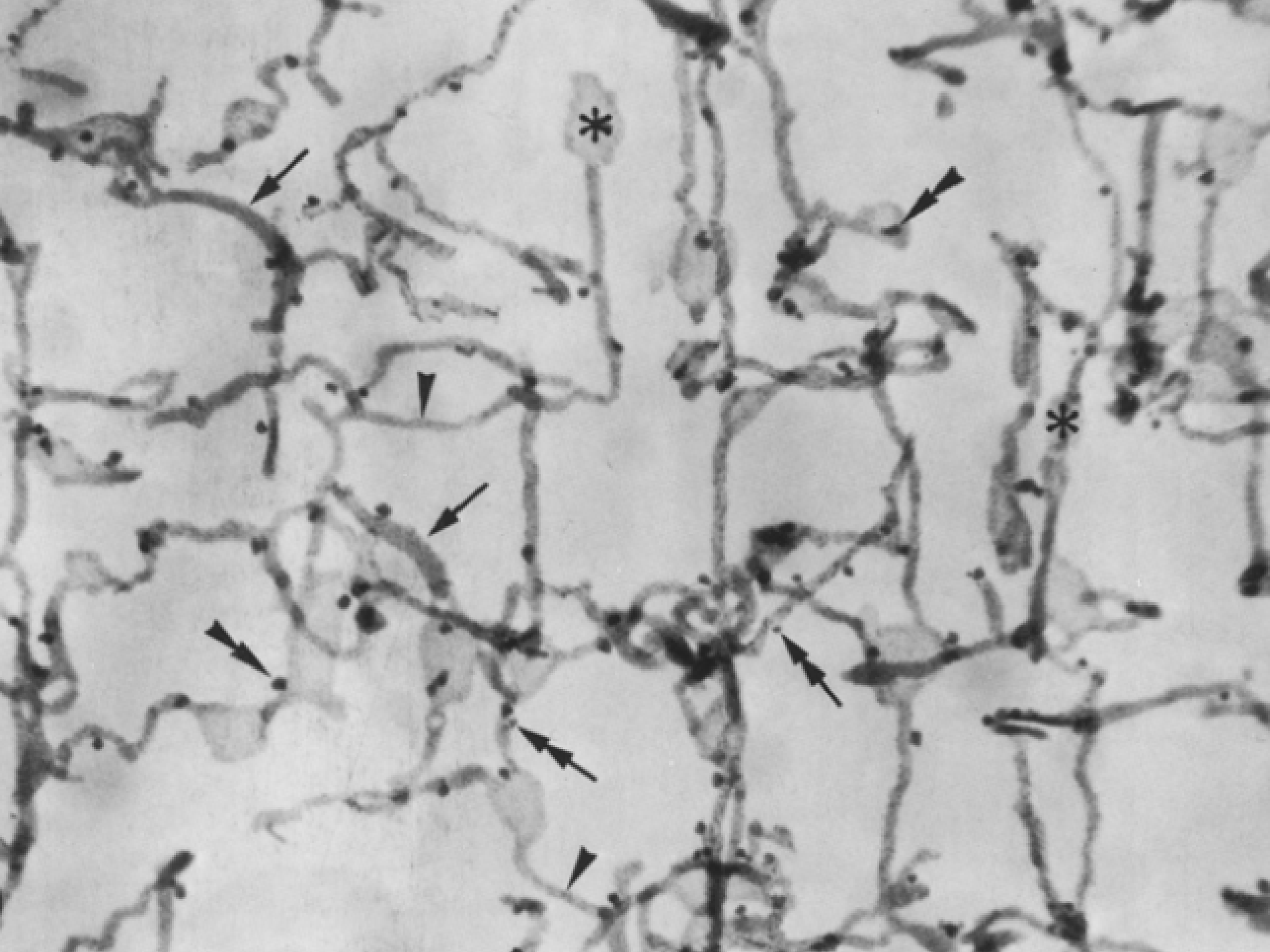
1981-1988: 外科病理学 名古屋大学大学院

1982-1987: **細胞生物学** 岡崎国立共同研究機構 生理学研究所

1988-2005: 外科病理学、特にリンパ腫病理学 愛知県がんセンター中央病院

2005-現在: 外科病理学、特にリンパ腫病理学 名古屋大学医学部附属病院

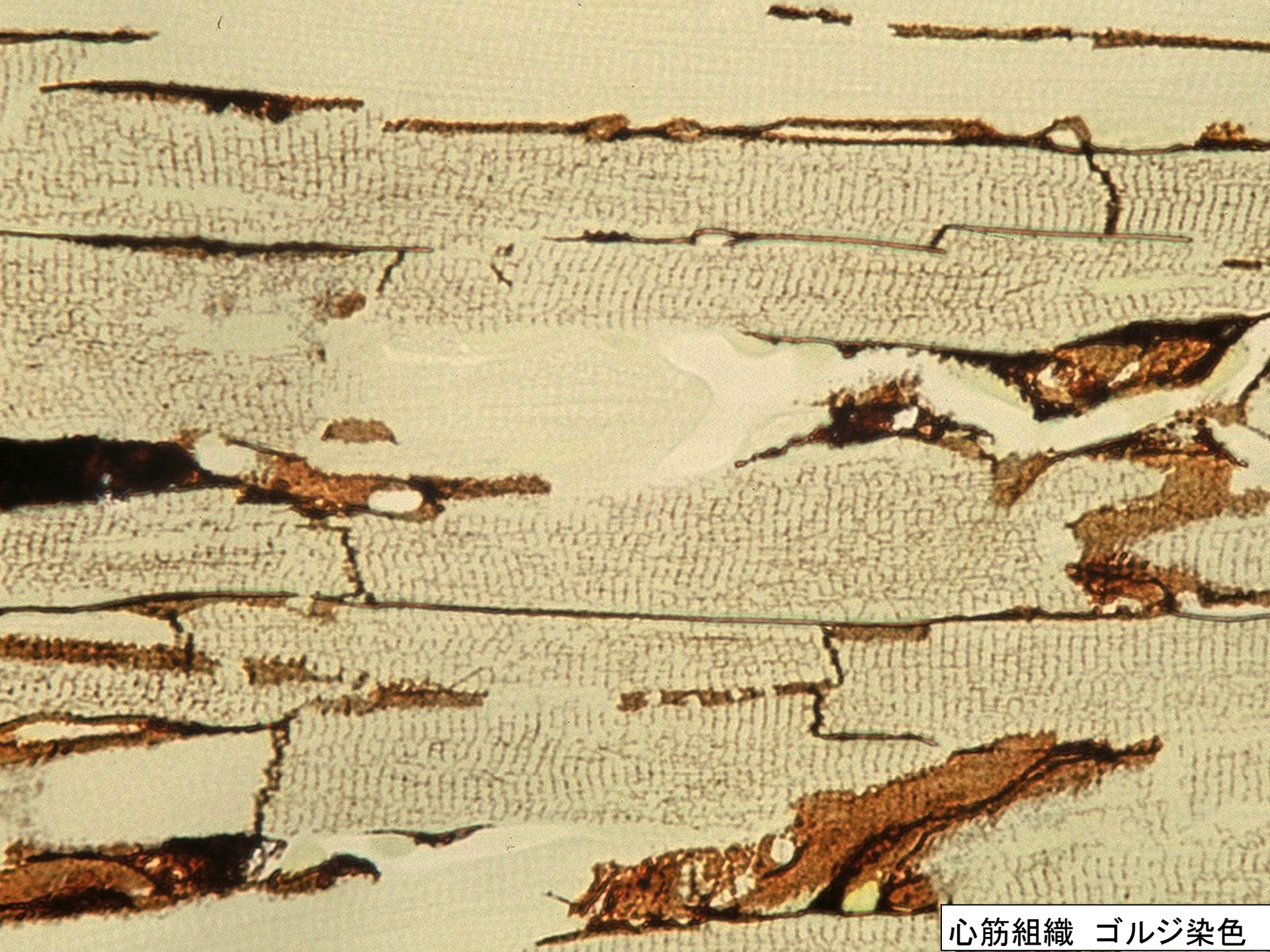




# これは何ですか？

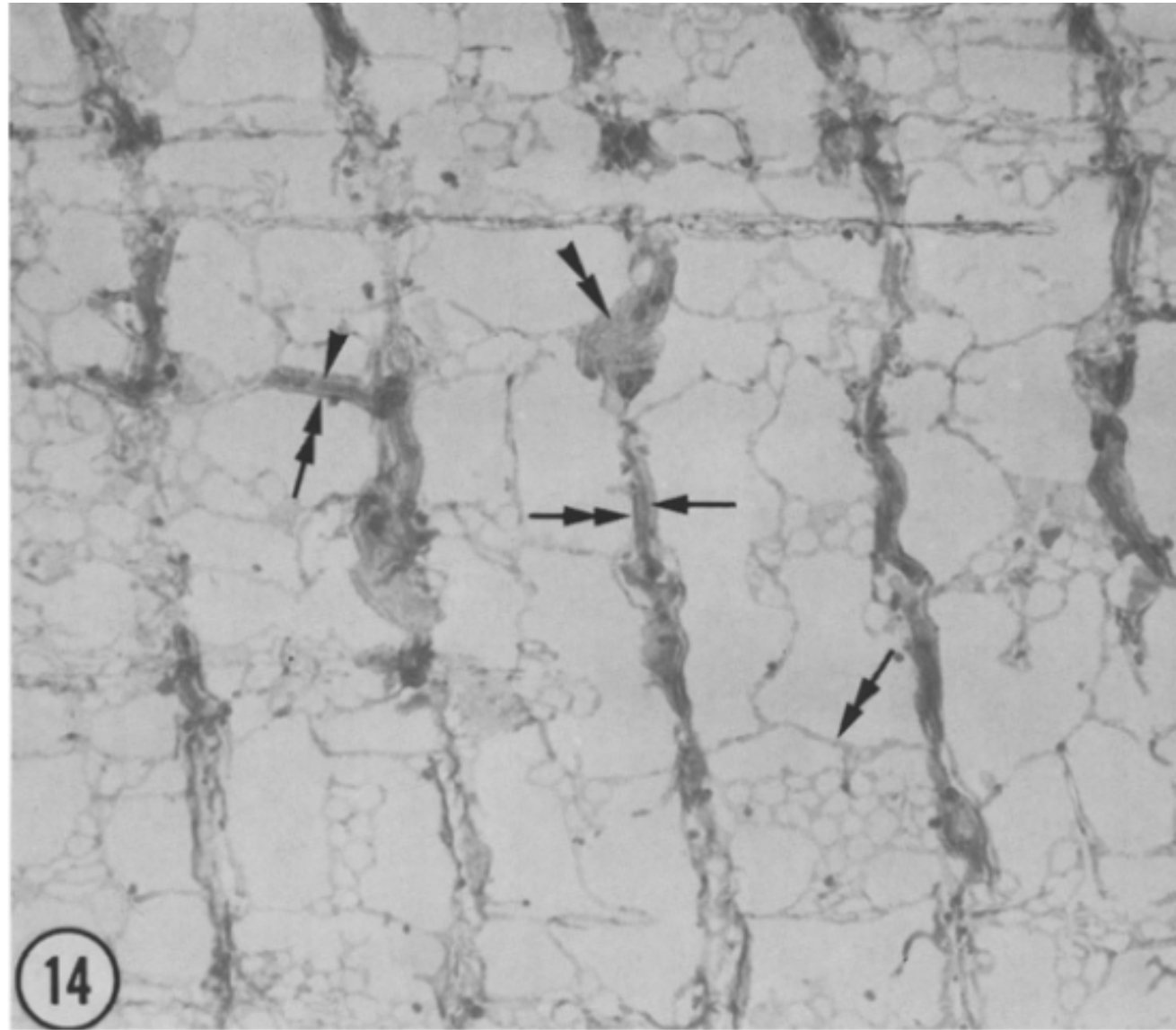
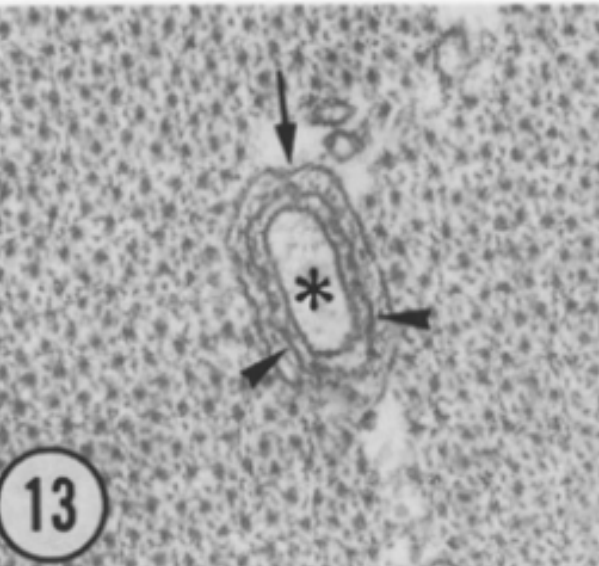
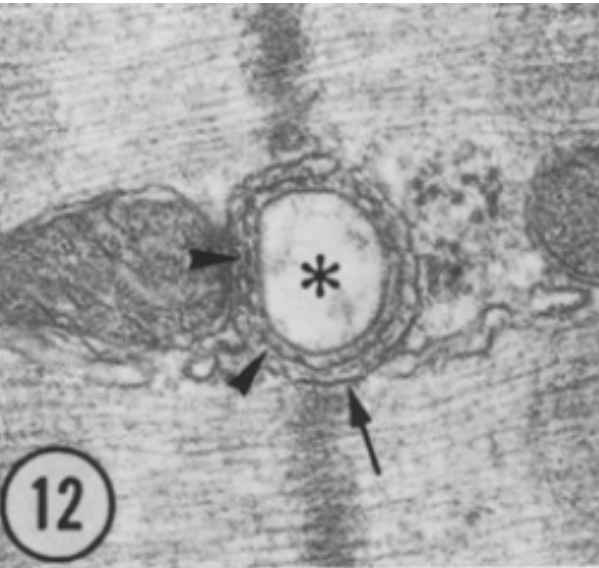
- 1) 血管
- 2) リンパ管
- 3) 類洞
- 4) 神経
- 5) 細胞内器官





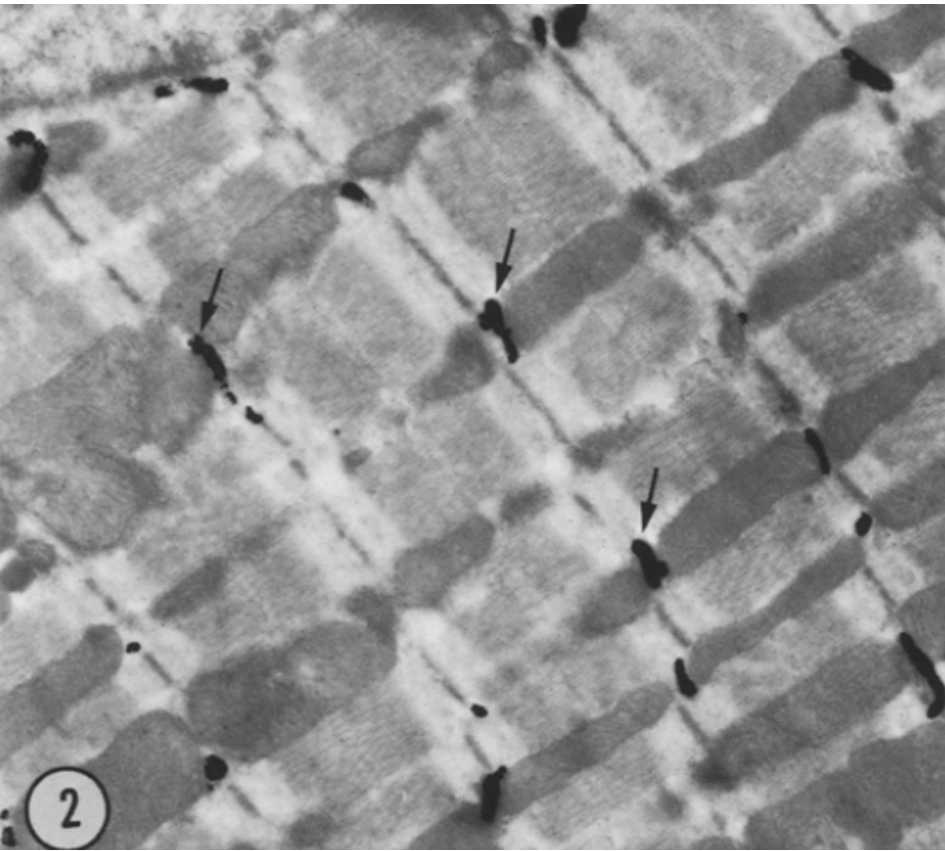
心筋組織 ゴルジ染色



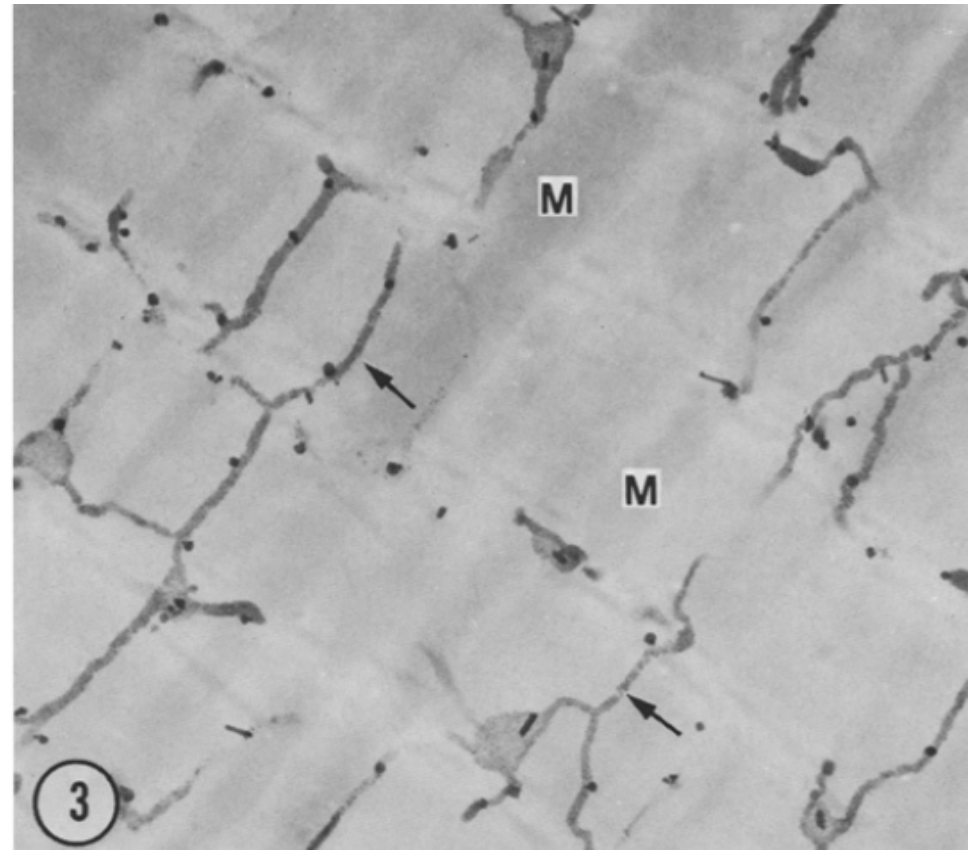


\* Transverse tubule

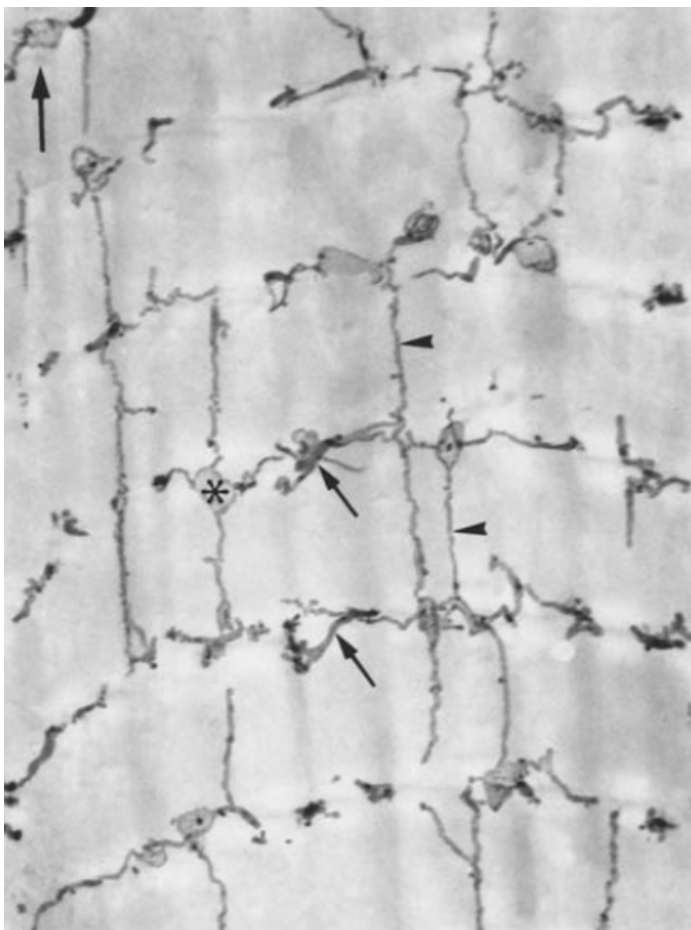
Sarcoplasmic reticulum (double arrow)



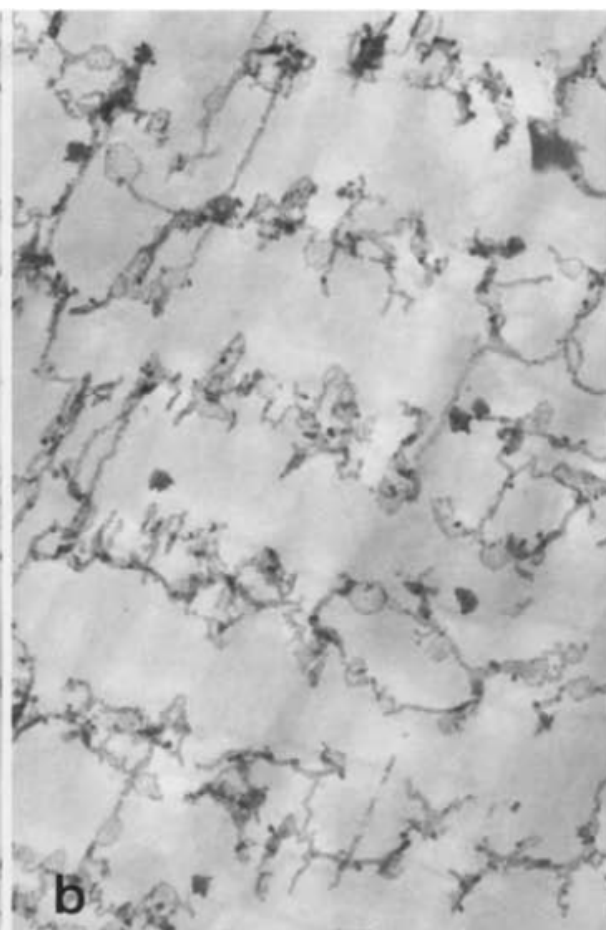
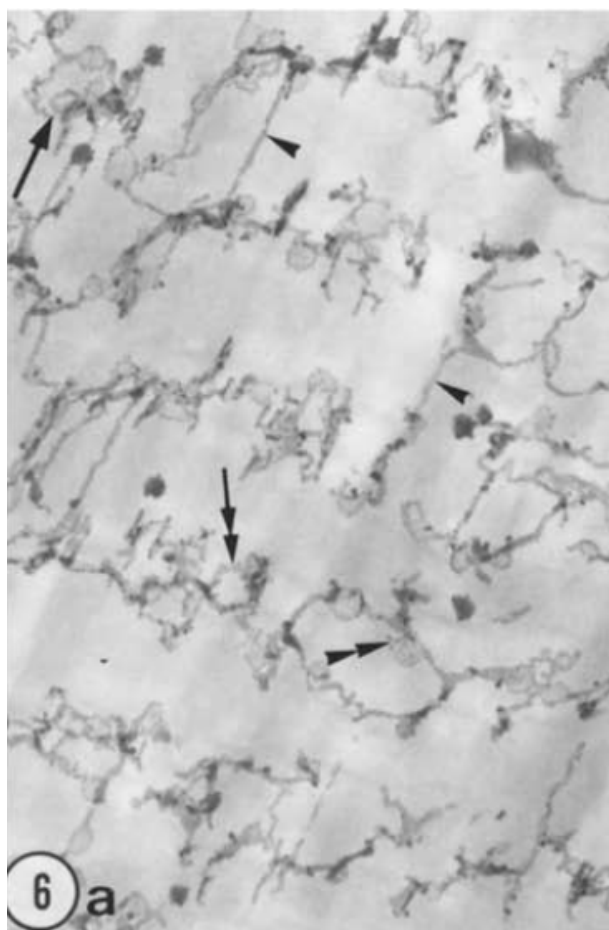
0.1 $\mu\text{m}$  in thick



1 $\mu\text{m}$  in thick



1 $\mu$ m in thick



3 $\mu$ m in thick

Tilting angle of  $\pm 8^\circ$  for the stereo views

Wister Rat





<https://home.hiroshima-u.ac.jp/seiri1/lab/index.html> 2020/6/5

入澤 宏 先生  
生理学

東京慈恵医科大卒

広島大学教授  
生理学研究所教授  
昭和61年 第一回上原賞



[https://brh.co.jp/s\\_library/interview/15/](https://brh.co.jp/s_library/interview/15/) 2020/6/5

濱 清 先生  
解剖学・細胞生物学

九州大卒

広島大学教授  
大阪大学教授  
東大医科研教授  
生理学研究所教授・所長  
岡崎国立研究機構長

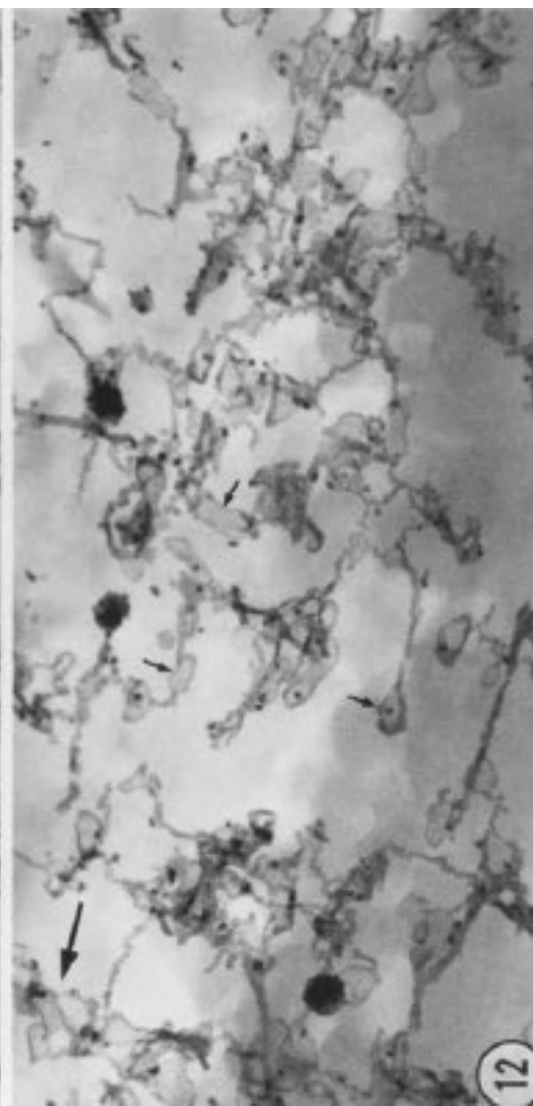
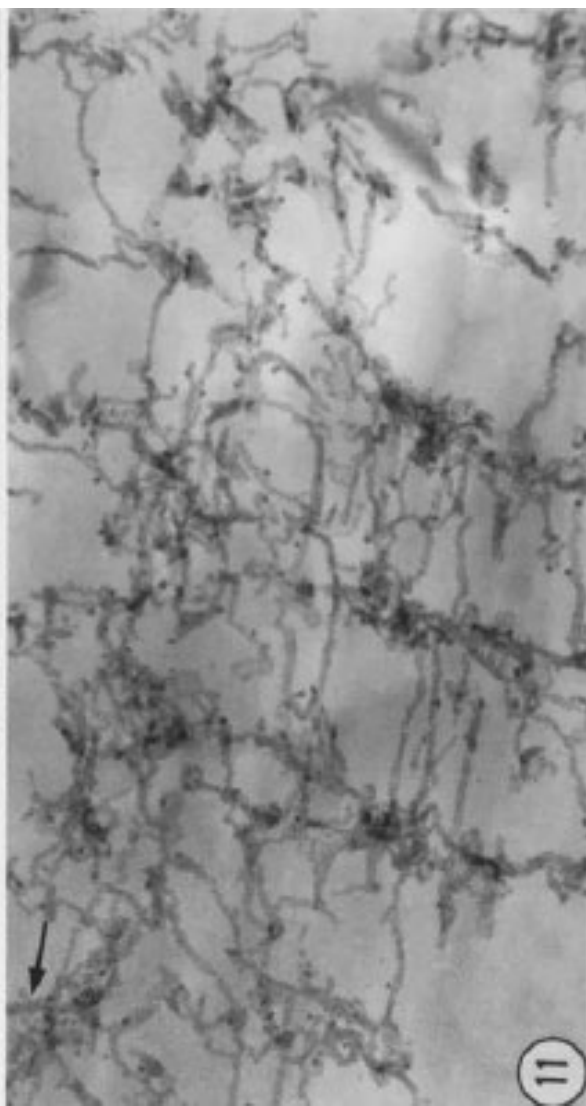
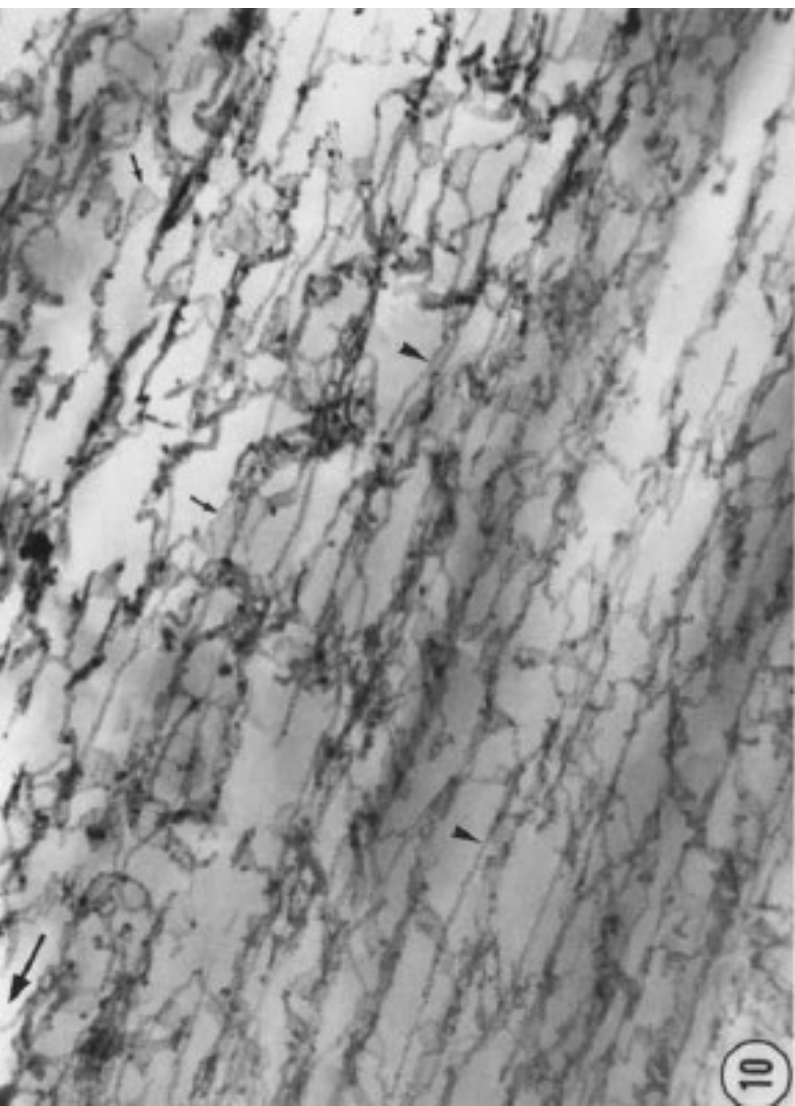


<https://www.jsltr.org/journal/44-1/4401mourn.pdf> 2020/6/5

飯島 宗一 先生  
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名古屋大卒

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名古屋大学教授  
名古屋大学総長  
第24回日本医学会総会会頭

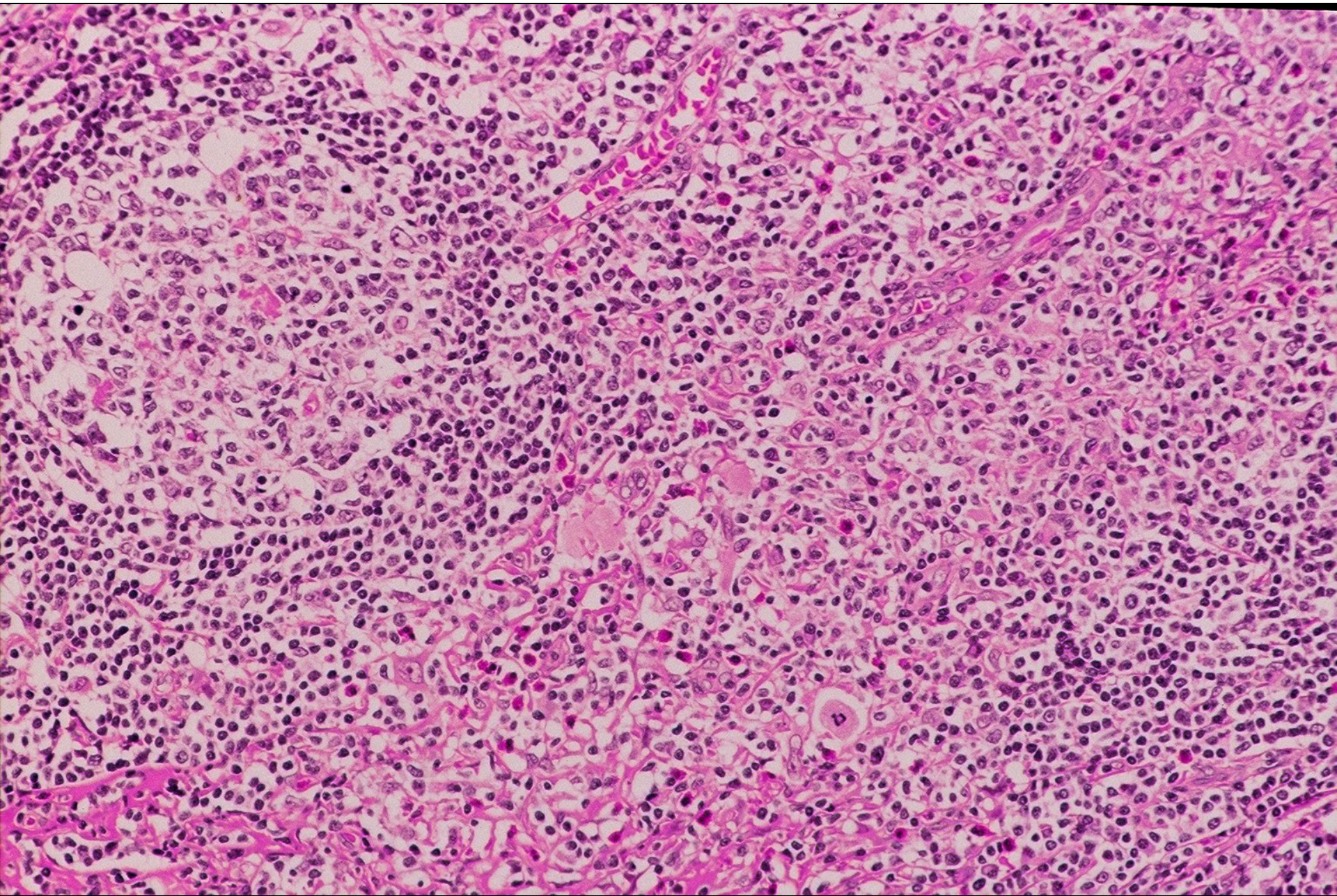


SHR Rat 自然高血圧発症ラット

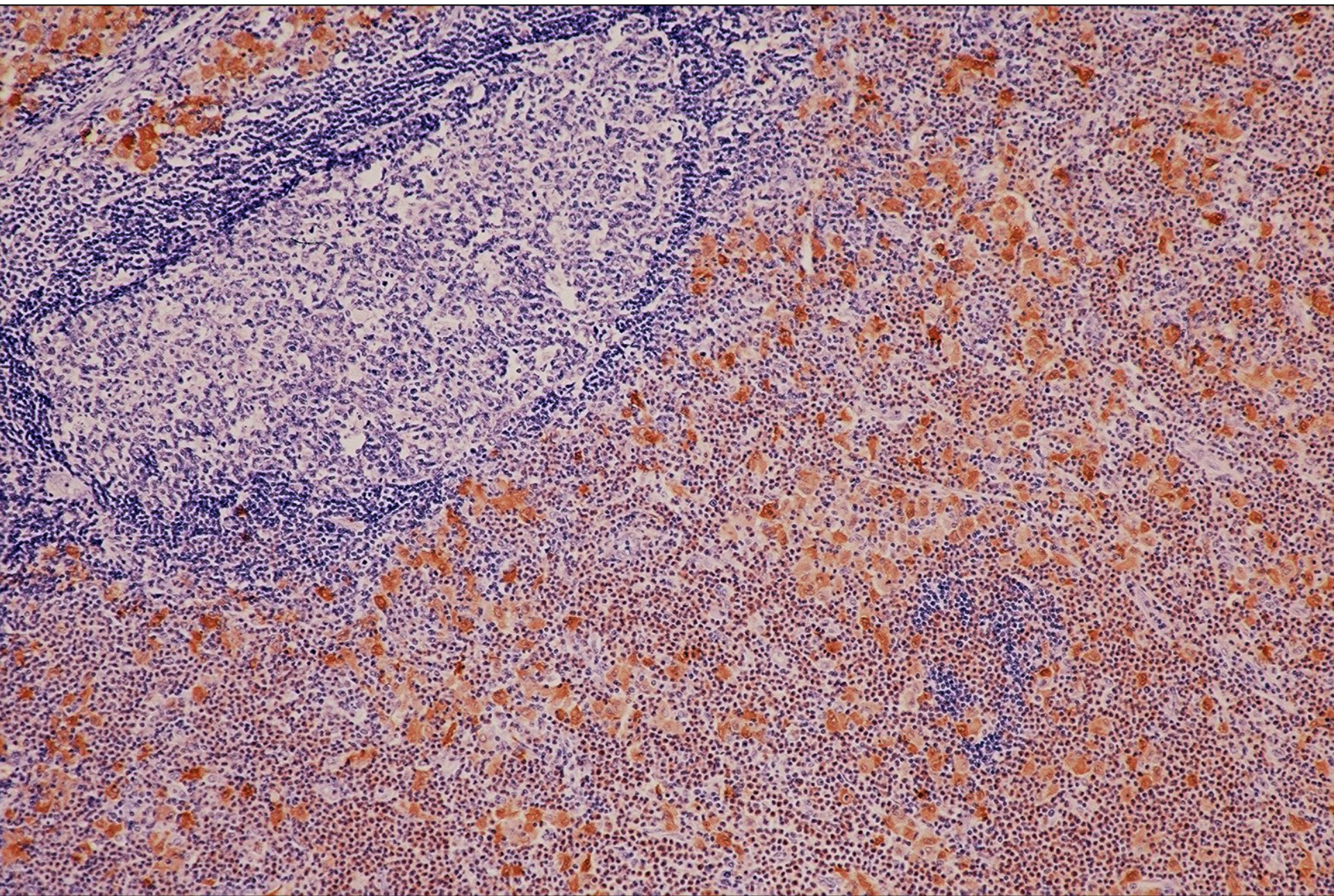
# Interdigitating Dendritic Cell Sarcoma (*Nakamura S et al. Cancer 1988;61:2562*)

- 指状嵌入樹状細胞肉腫、極めてまれな腫瘍
- 58歳男性、1982年、左頸部リンパ節の腫脹を主訴に来院、生検診断は悪性リンパ腫、分類不能型、ただしホジキンリンパ腫との鑑別が問題となる。CHOPにて治療するも、1986年、空腸に二度にわたり再発、外科的切除、腸間膜リンパ節に浸潤を伴う。
- 1990年、肺炎にて死亡、診断より101ヵ月。
- 遺言により剖検を施行、腫瘍残存なし



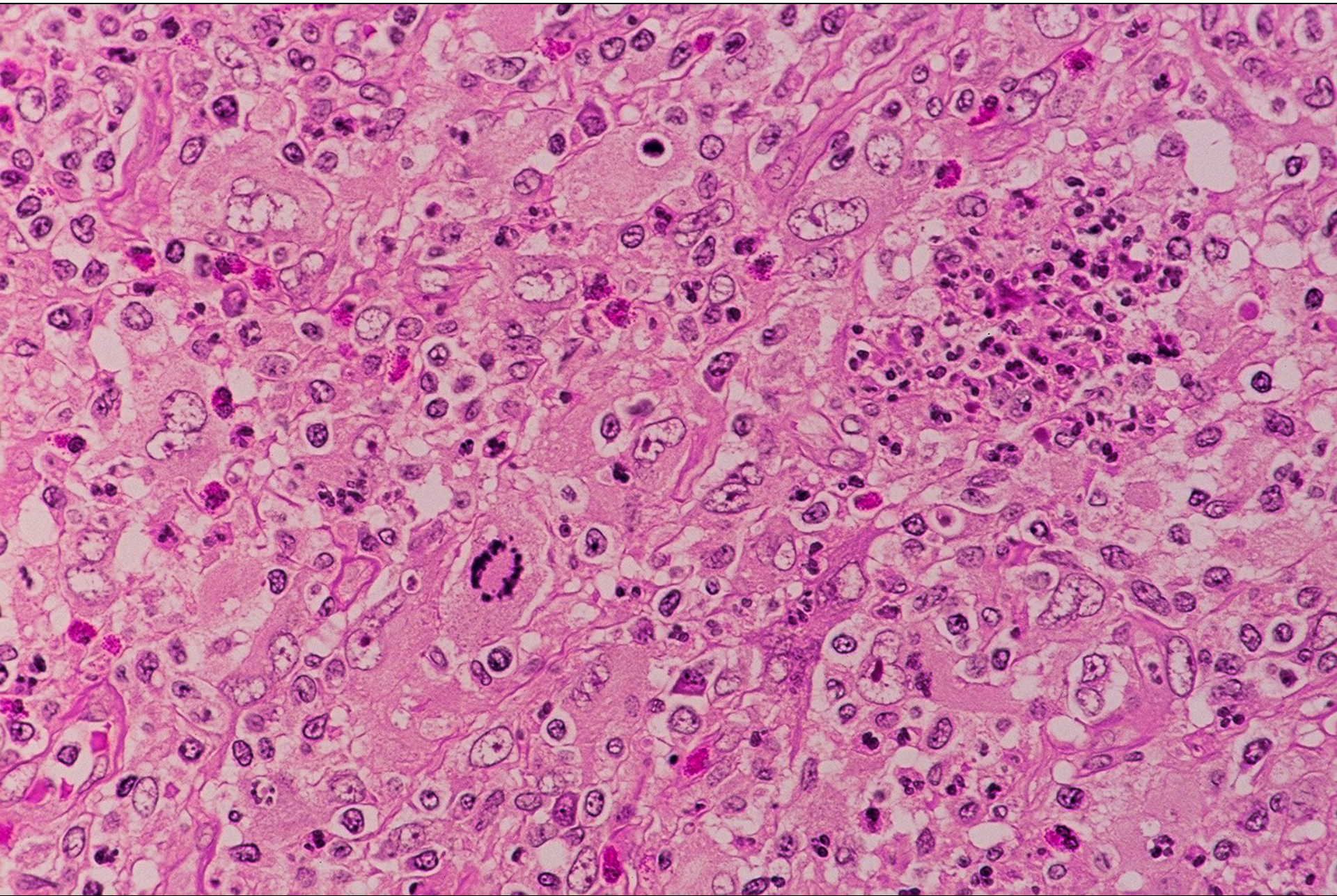






**S100**

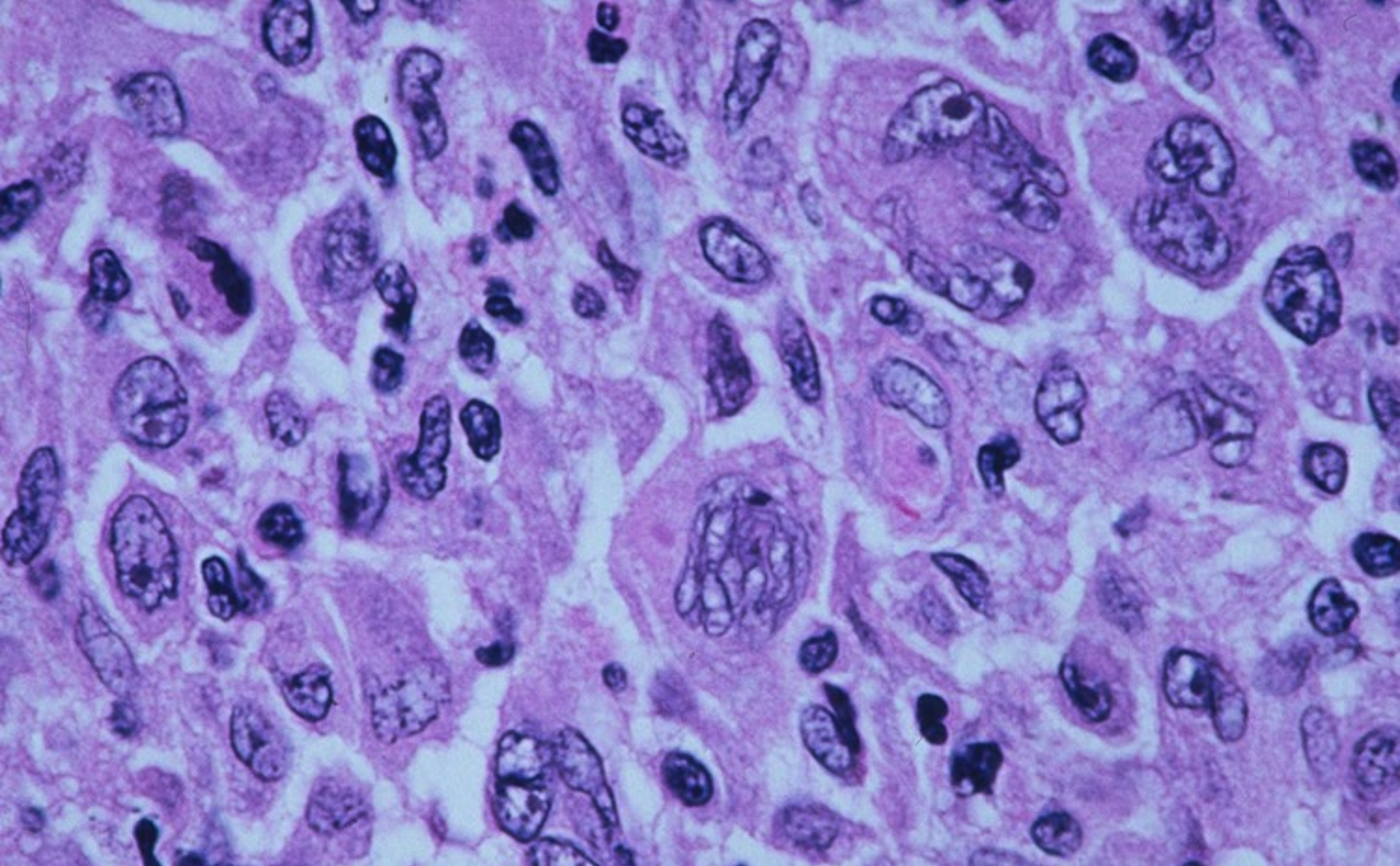






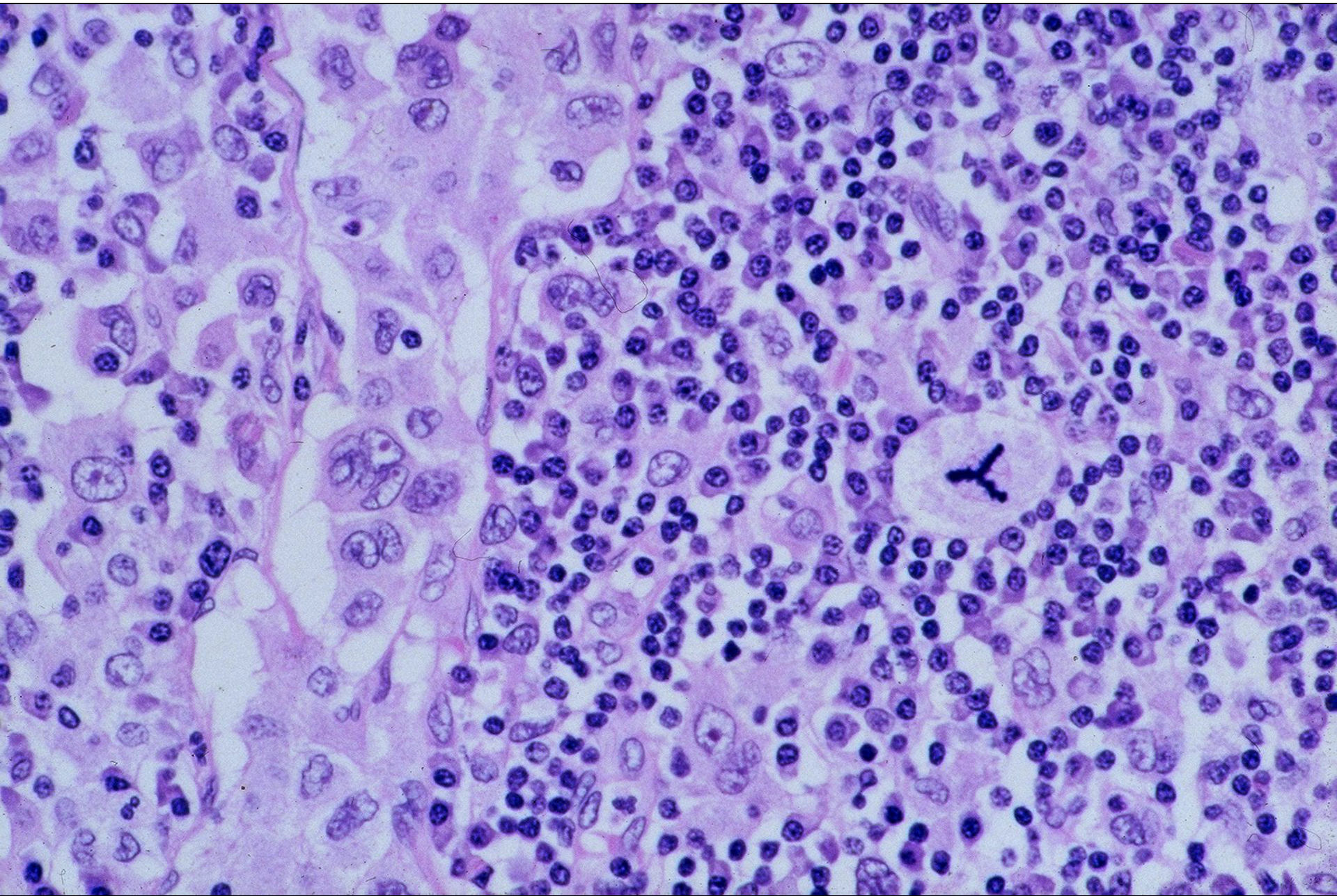




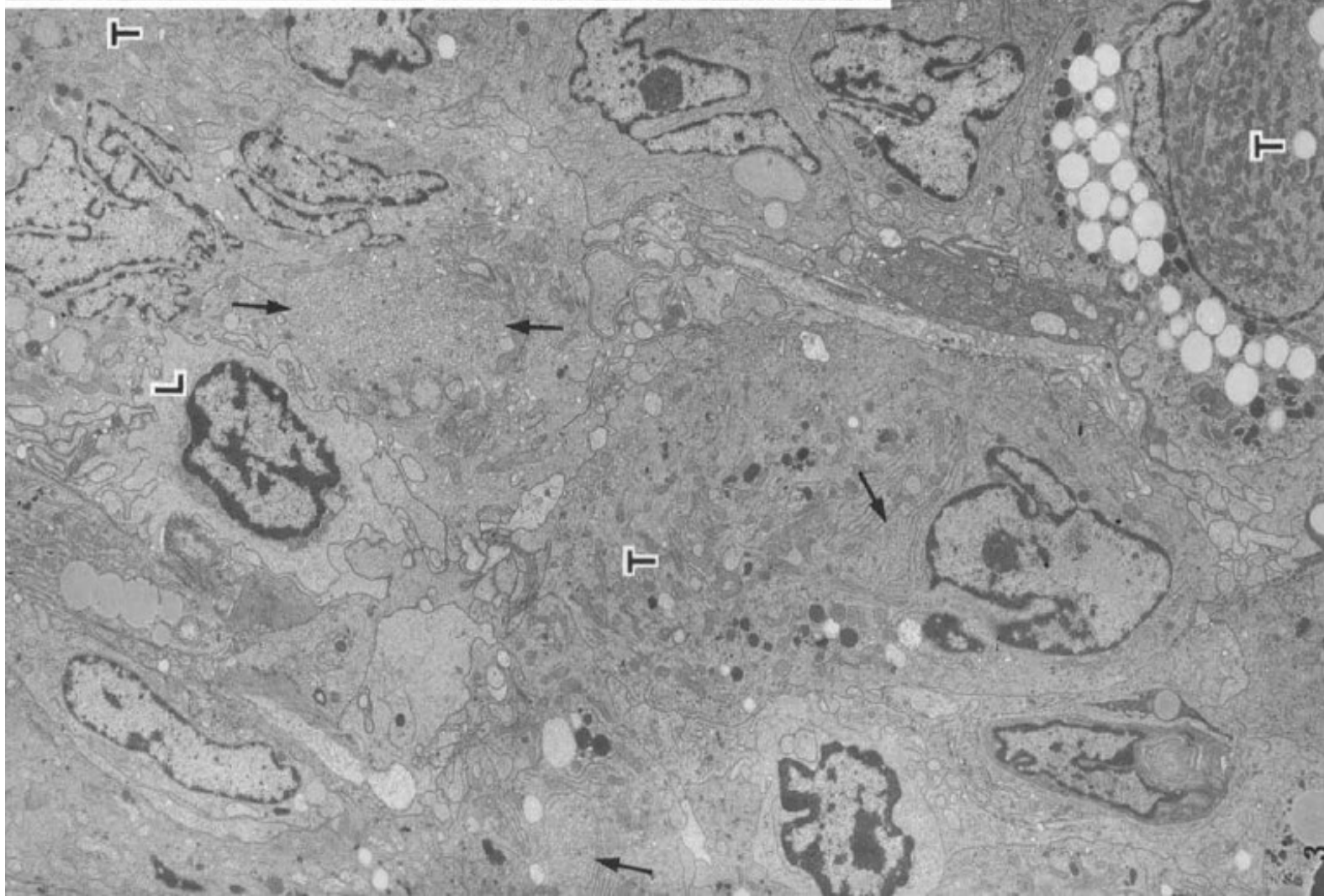
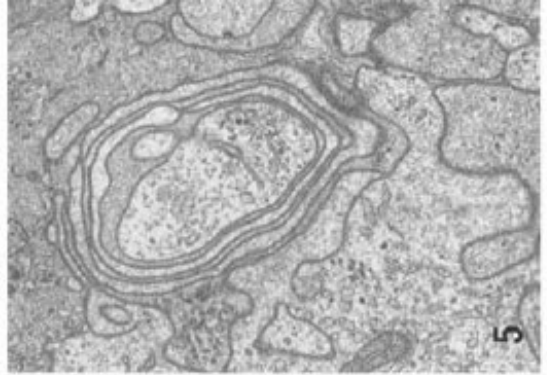
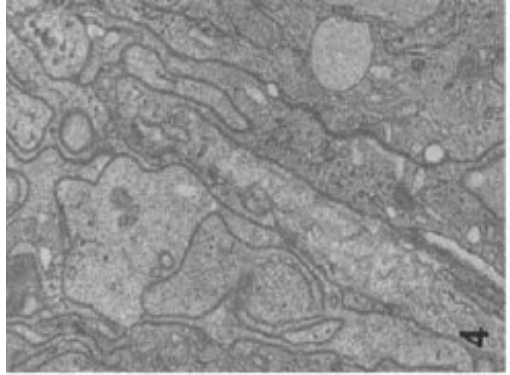


The tumor cells are positive for CD4, CD68, CD163 and S100 protein, but not for CD1a, CD34, Langerin or markers of follicular dendritic cells, B-cell- or other T-cell associated antigens

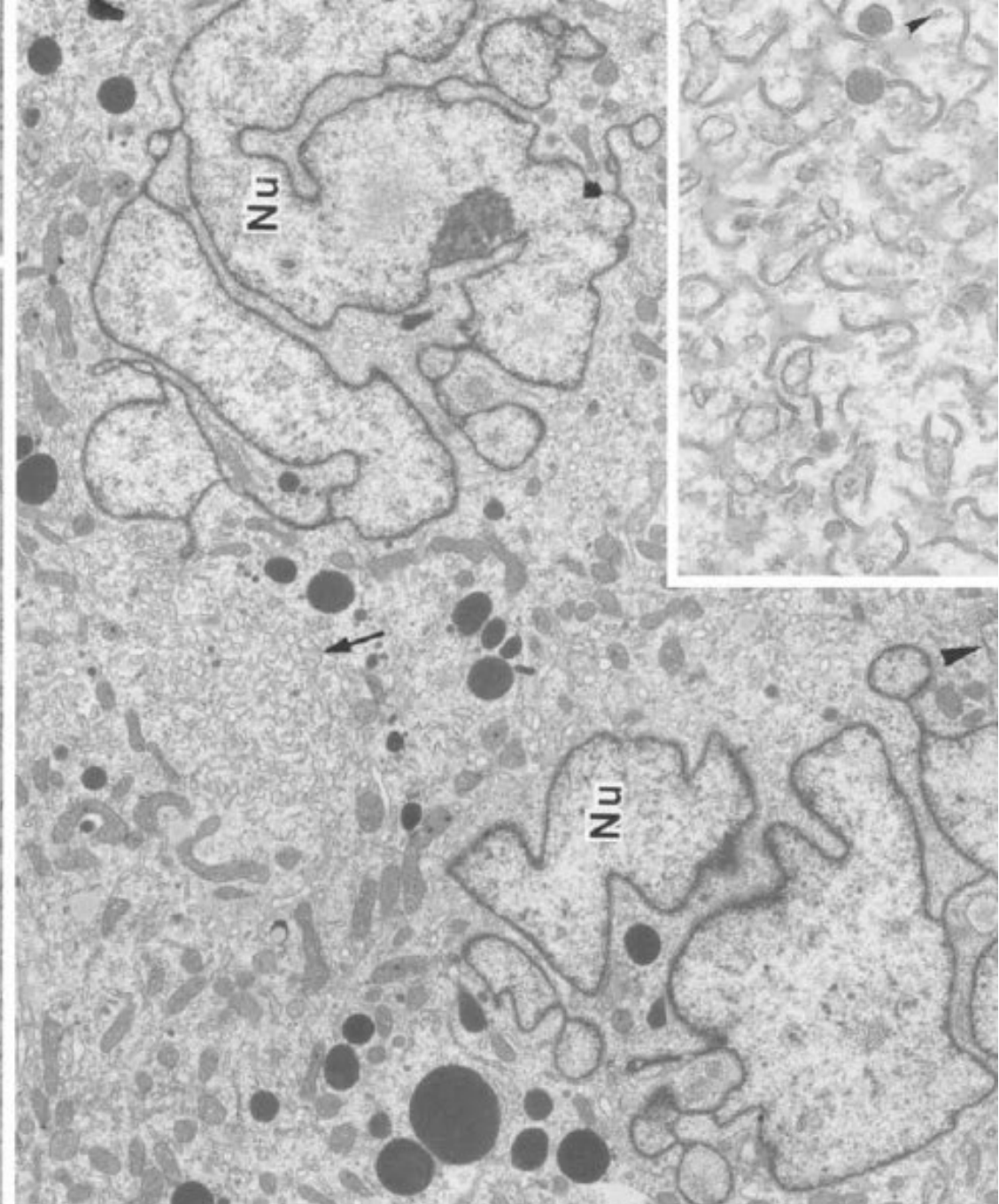
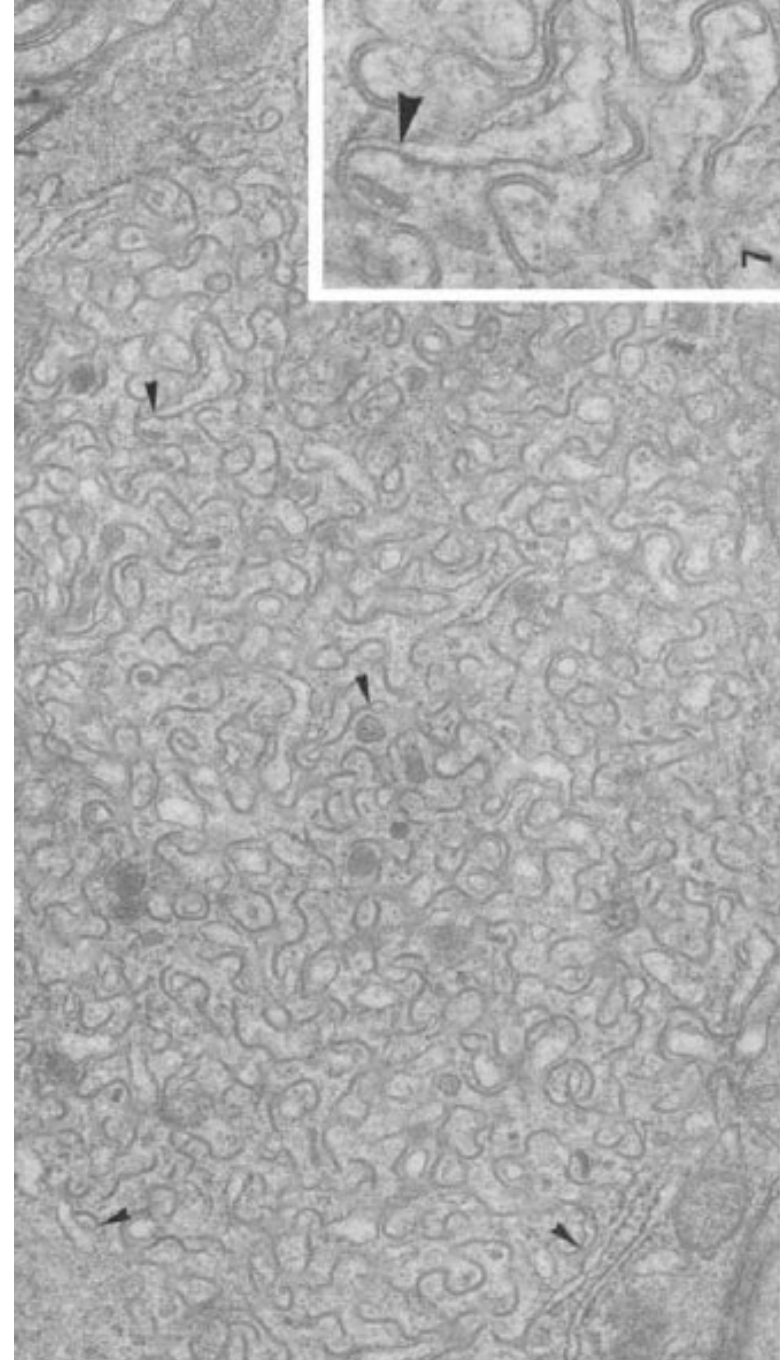




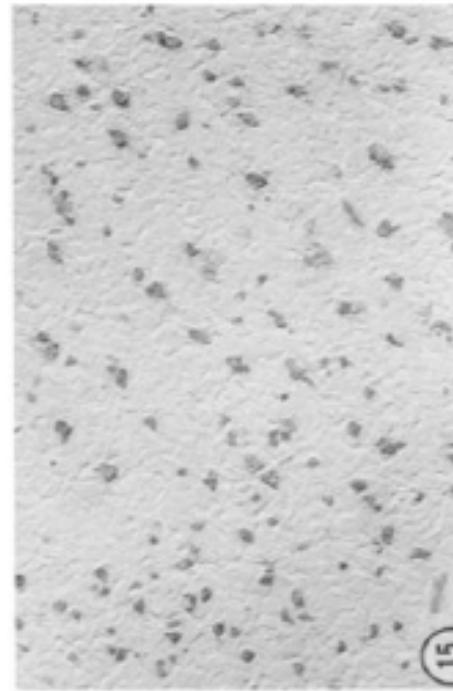
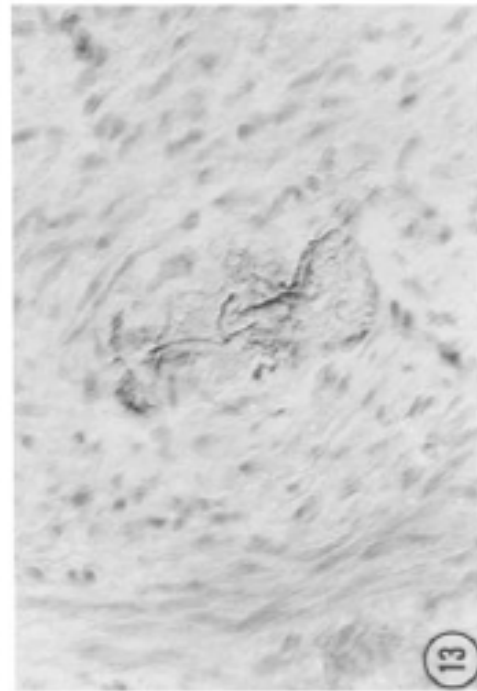
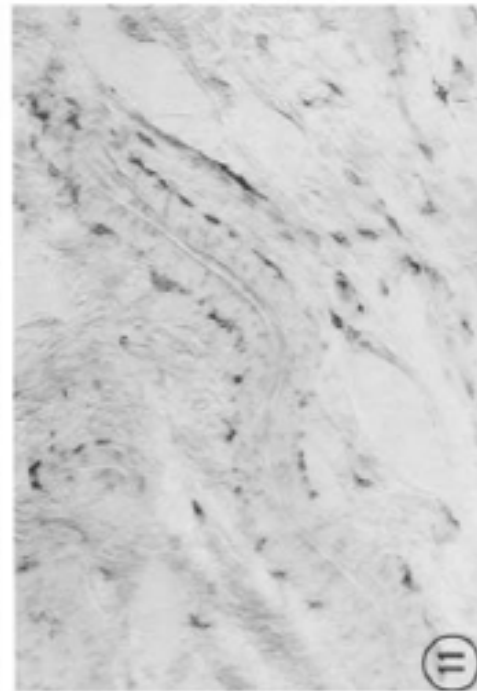
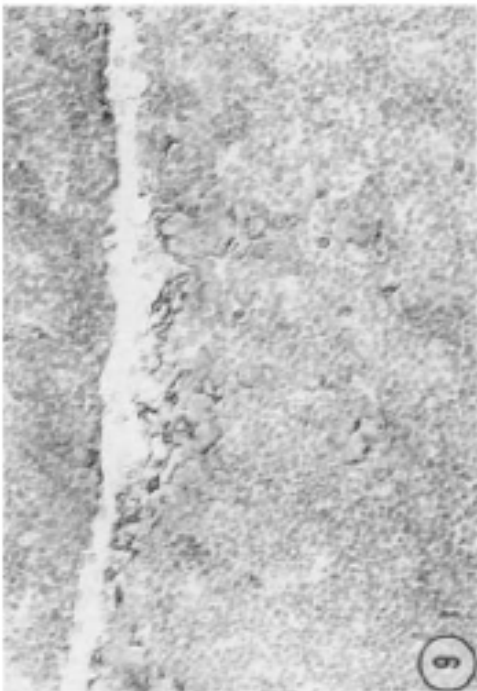
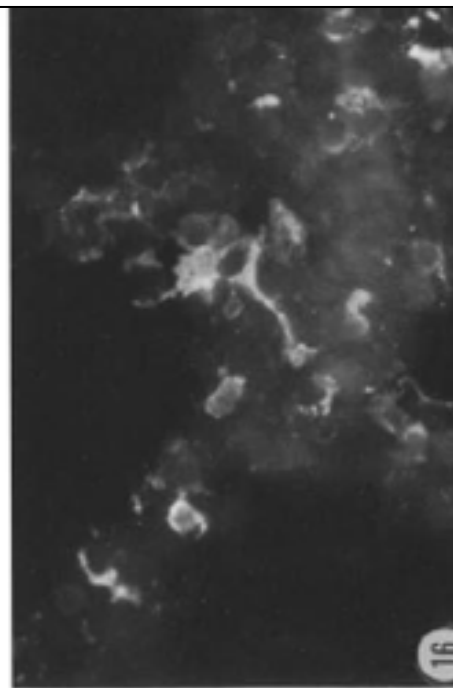
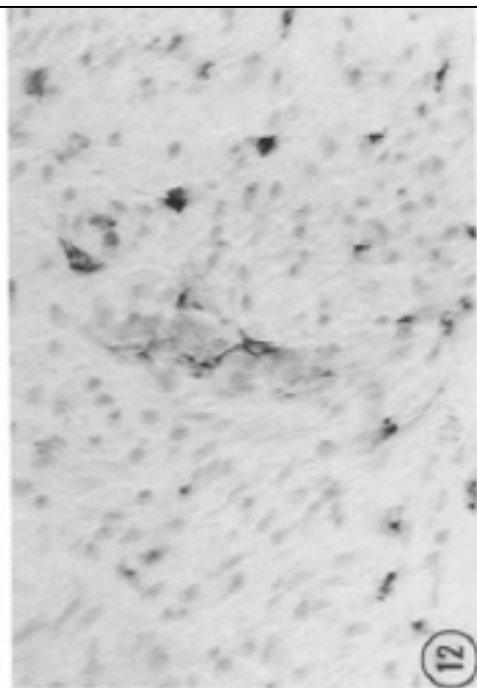
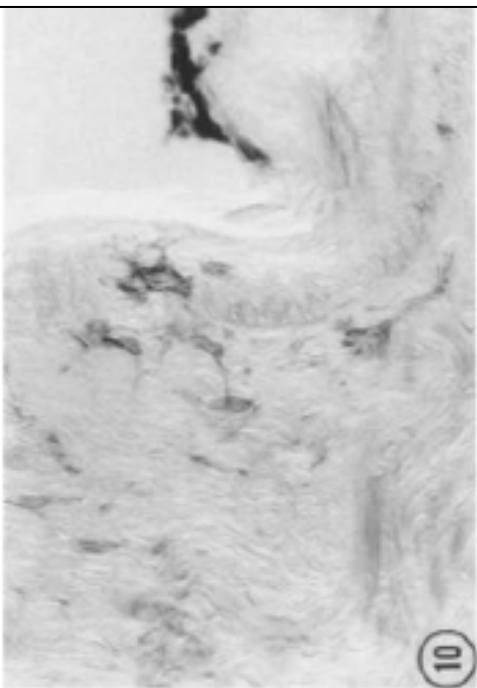




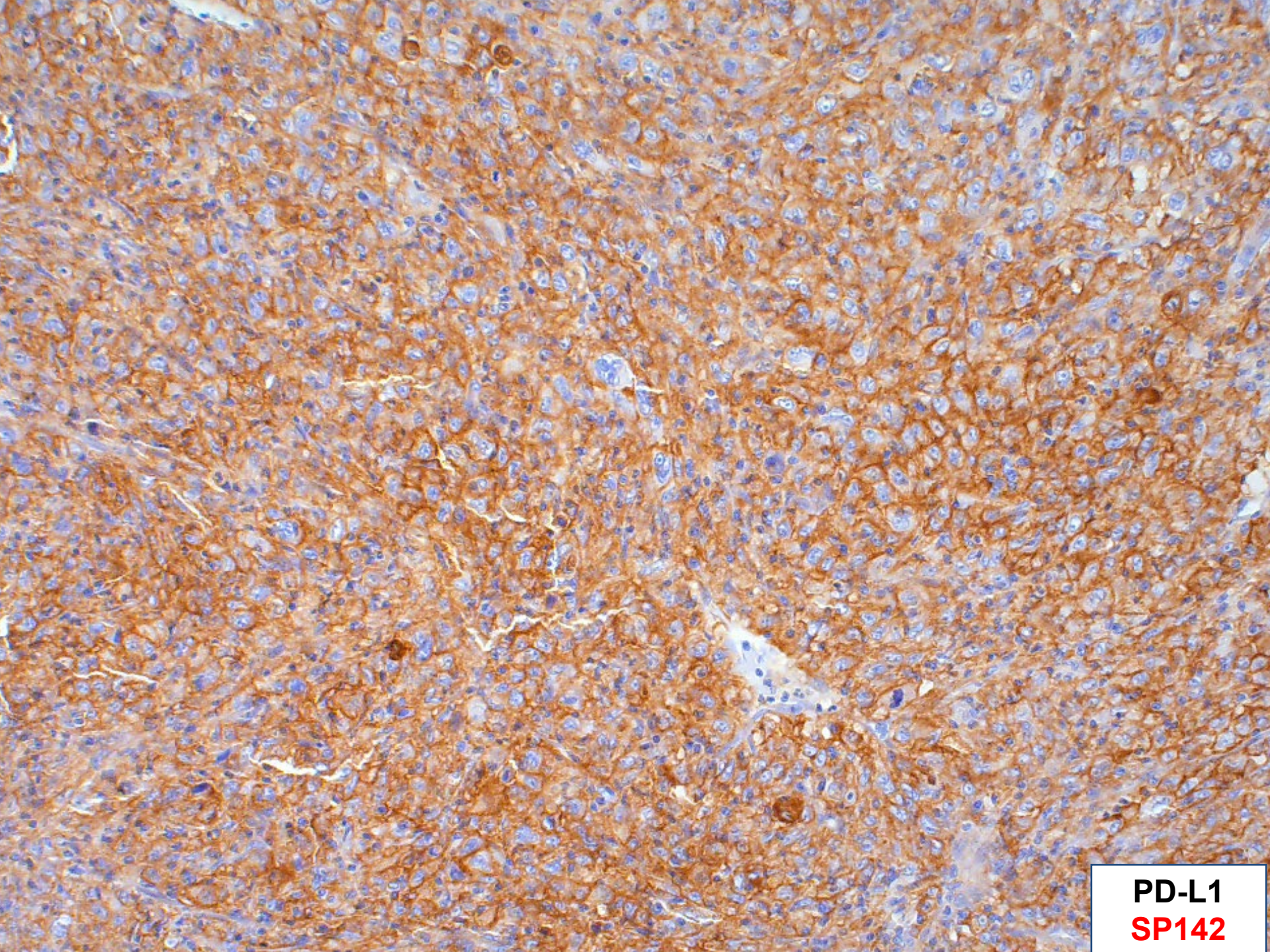




Ribosome-Lamella Complex

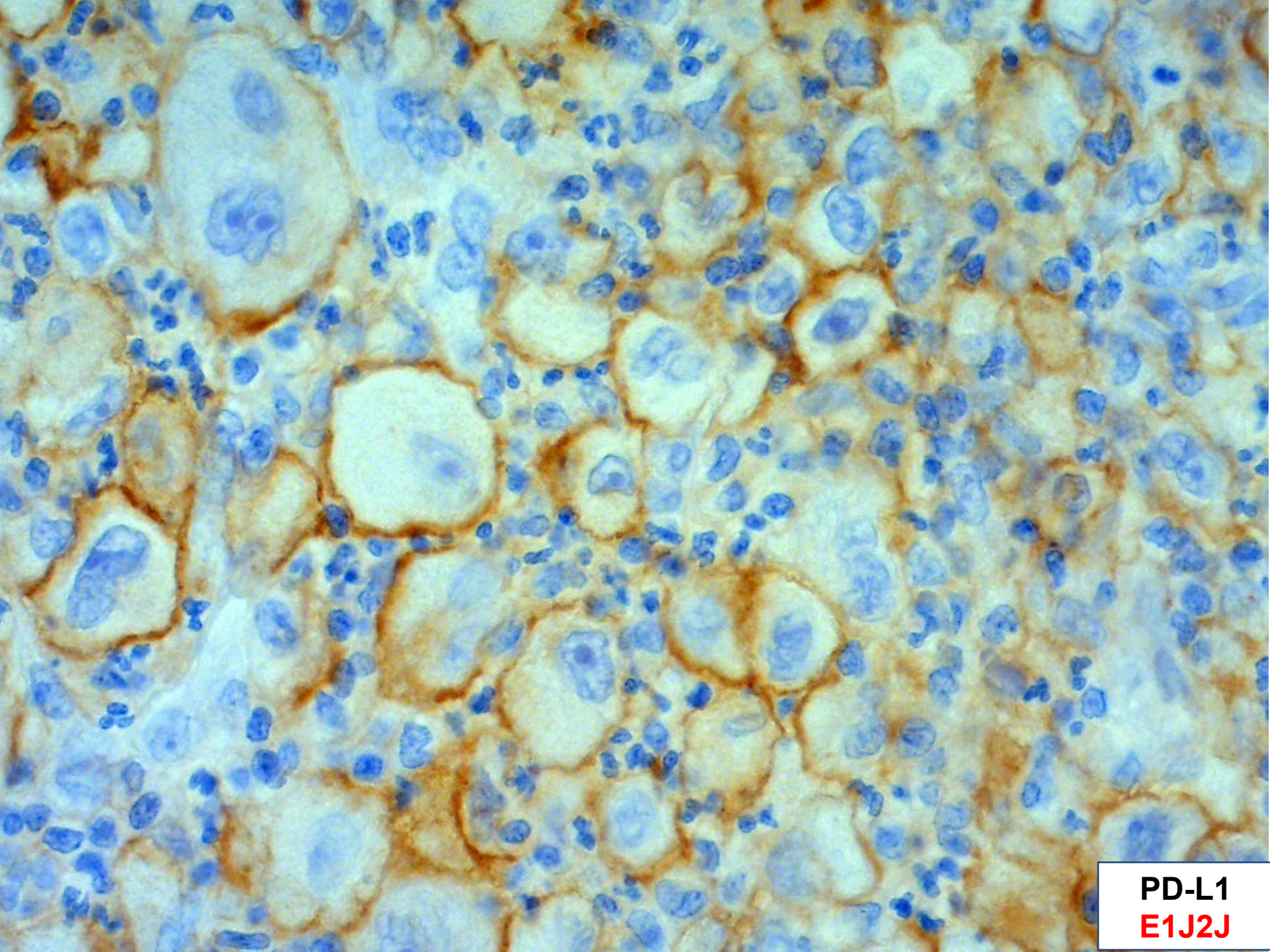






**PD-L1**  
**SP142**





**PD-L1**  
**E1J2J**

# Interdigitating Dendritic Cell Sarcoma

*(Nakaumra S et al. 1988~2018)*

- Interdigitating cell sarcoma. A morphologic, immunologic, and enzyme-histochemical study. *Cancer*. **1988** Feb 1;61(3):562-8. PMID: 3338024
- Observation on the fine structure of interdigitating cell sarcoma. *Virchows Arch A Pathol Anat Histopathol*. **1989**;414(2):121-8. PMID: 2492691
- Interdigitating cell sarcoma (ICS). Evidence of interdigitating cell origin, immunocytochemical studies with monoclonal anti-ICS antibodies. *Virchows Arch A Pathol Anat Histopathol*. **1989**;415(5):447-57. PMID: 2508304
- Imprint cytology and immunohistochemical study of interdigitating cell sarcoma. *Cytopathol*. **1991**;7(5):553-5. PMID: 1954841
- Interdigitating cell sarcoma: a morphologic and immunologic study of lymph node lesions in four cases. *Pathol Int*. **1994**;44(5):374-86. PMID: 8044307
- Neoplastic PD-L1 expression on interdigitating dendritic cell sarcoma: a supplementary study of a case report. *Pathol Int*. **2018**;68(10):577-578. PMID: 30094900





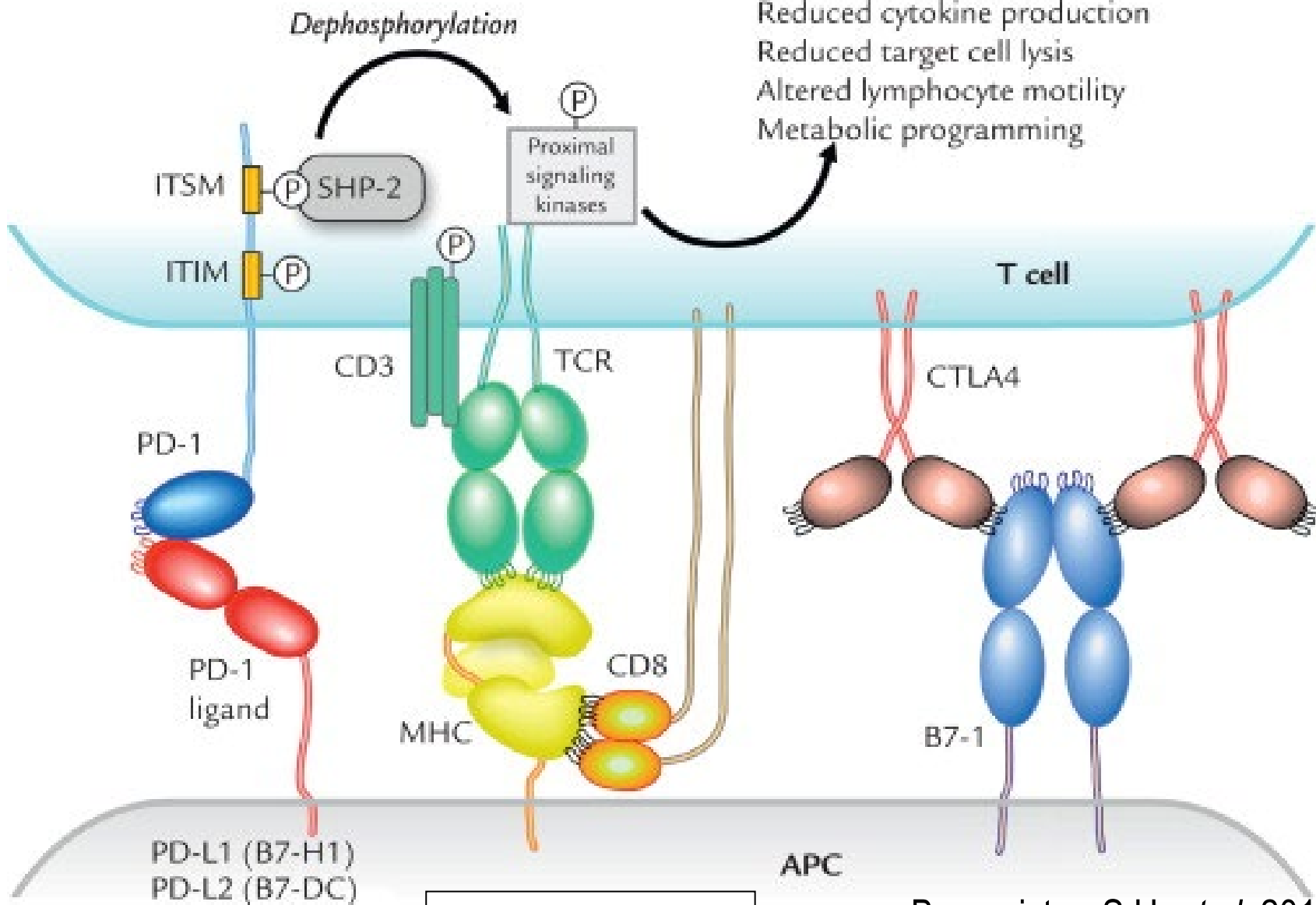
須知 泰山 先生  
病理学(生理学) 名古屋大卒

愛知県がんセンター病院臨床検査部 部長



# PD-1+ cells

Reduced TCR signaling  
Reduced cytokine production  
Reduced target cell lysis  
Altered lymphocyte motility  
Metabolic programming



# PD-L1+ cells

Baumeister, S.H. *et al.* 2016;  
*Annu. Rev. Immunol.* 34:539-73



CHL is now regarded as a prototypic  
immune escape-based disease.

PD-L1 alteration is a defining feature of cHL.  
*Shipp MA, ISHL11, Oct. 27, 2018, Cologne, Germany*

PD-L1 on NSHL, EBV-negative



# Diffuse Large B-cell Lymphoma

今、何が問題か？

- ・ ホジキンリンパ腫の再定義
- ・ DLBCLにおける**免疫逃避**と**免疫不全**の評価
- ・ 節外性DLBCLの特殊性の再評価

腫瘍細胞と背景細胞におけるPD-L1発現  
の意義は異なる

古典型ホジキンリンパ腫はPD-L1変異とPD-L1発現に依拠する“免疫逃避”を基盤とするB細胞腫瘍である

## 要点

- ホジキンリンパ腫の再定義、形態から“免疫逃避”
- “免疫逃避”は、PD-L1発現により定義される
- ホジキンリンパ腫の診断にPD-L1検索は必須である
- ホジキンリンパ腫の定義の変更は、**非ホジキンリンパ腫**の再評価と再定義を促す



# Varied Basis for Recognition of New Subtypes of Aggressive B-cell Lymphomas

- Cell of origin, gene expression profiling
  - ABC, GCB, PMBL, genetic subtypes
- Clinical factors
  - Primary CNS DLBCL, PMBL
  - Age, Chronic inflammation
- Etiological factors
  - EBV, HHV-8
- Molecular pathogenesis
  - *BCL6*, *MYC*, *ALK*, *BCL2*

Immune escape and immunodeficiency

# PD-L1発現の臨床病理学的意義： B細胞リンパ腫

## 要点

生物学的に異なる疾患スペクトラムの理解：次の3群に分けて考える必要がある

1. **前縦郭(胸腺)B細胞腫瘍**の特殊性：結節硬化型CHLと前縦郭(胸腺)原発大細胞型リンパ腫、およびそれらの中間型(灰色リンパ腫)
2. **EBV関連B細胞リンパ腫**の多様性：混合型CHL(EBV陽性)とEBV陽性びまん性大細胞型リンパ腫
3. **節外性**びまん性大細胞型B細胞リンパ腫特殊型

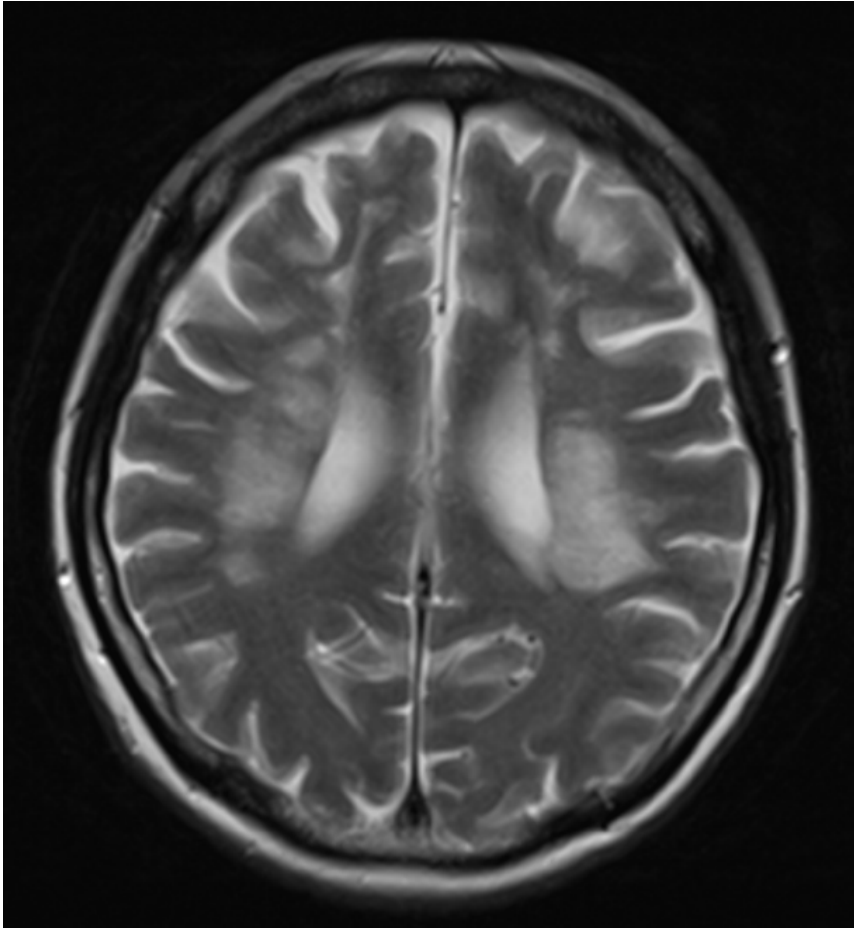


# A Case Presentation of IVLBCL with Neoplastic PD-L1 Expression

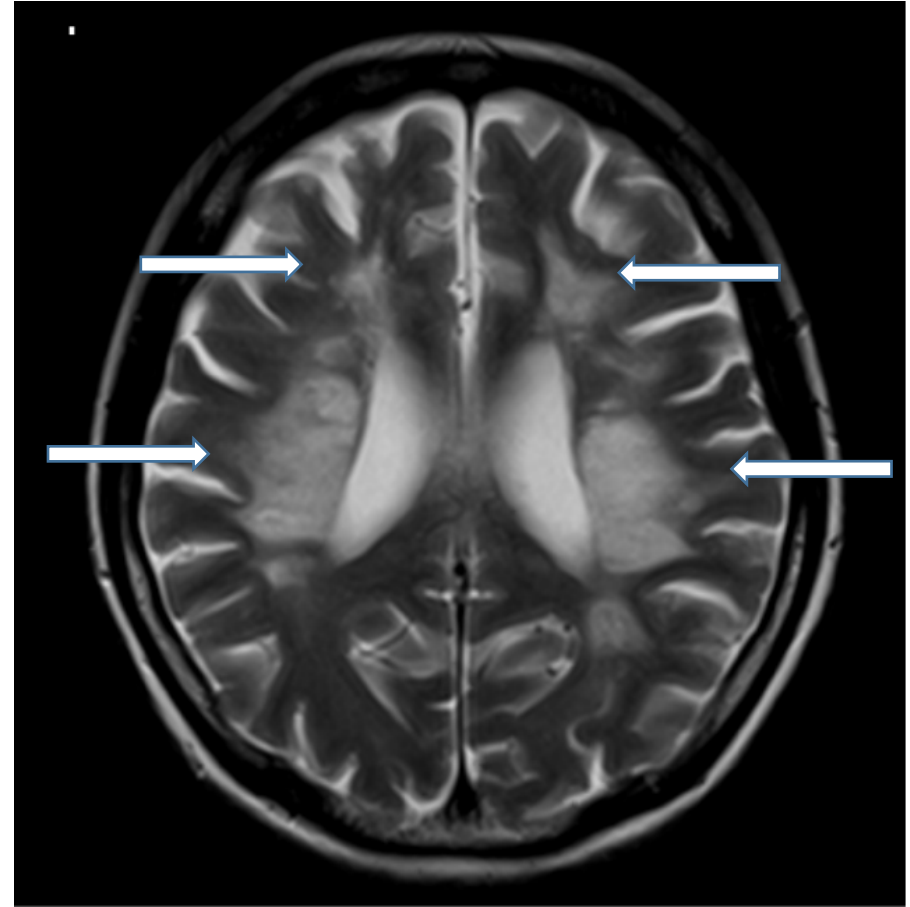
(Sakakibara A et al. J Clin EXP Hematop. 2018)

- 51歳女性
- 入院2月前より認知障害、失見当識、体幹失調
- 脳MRIにて多発梗塞巣、両側中大脳動脈の閉塞
- 全身検索にも拘わらず明確な診断困難、血管内大細胞型B細胞リンパ腫が疑われランダム皮膚生検を施行するも、結果は陰性
- 入院後3ヵ月で多臓器不全にて死亡、全経過を通してリンパ節腫脹なし
- 剖検を承諾された

# Cerebral Magnetic Resonance Imaging (MRI)



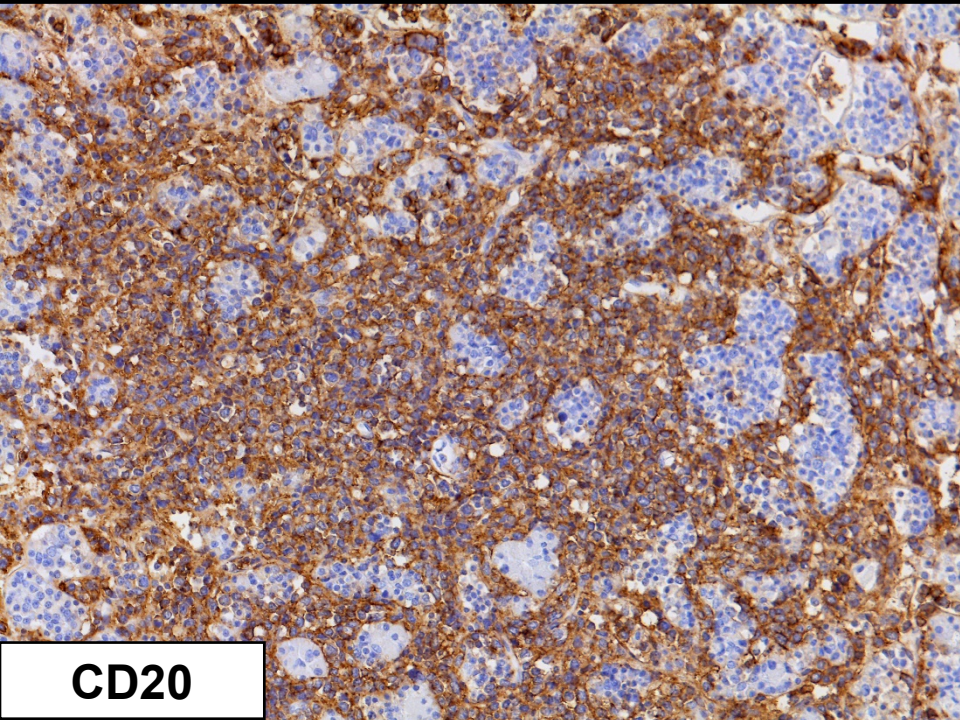
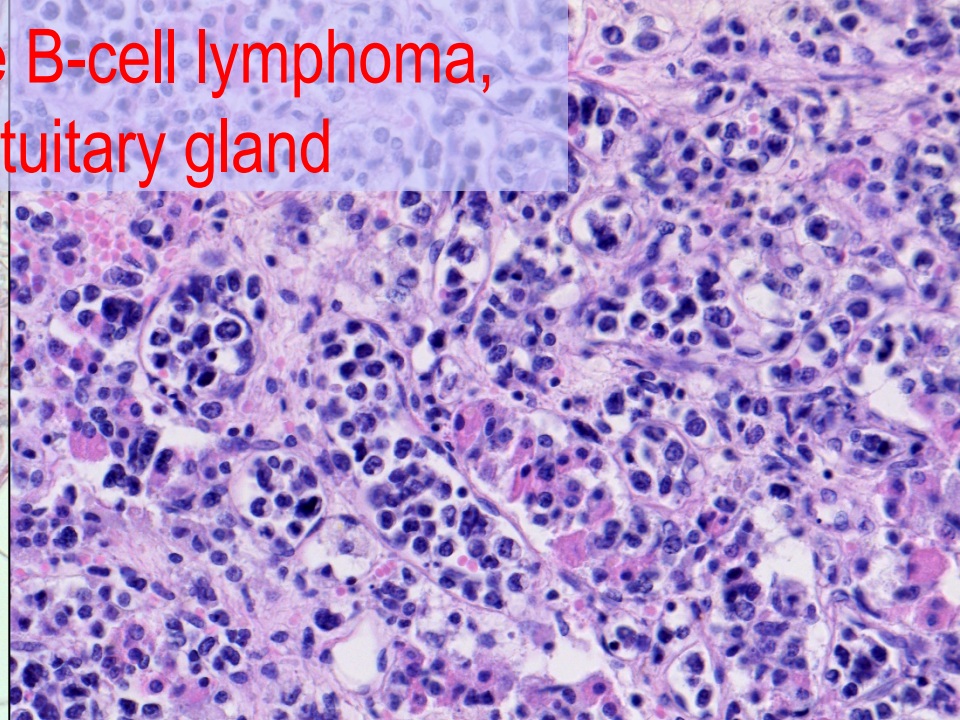
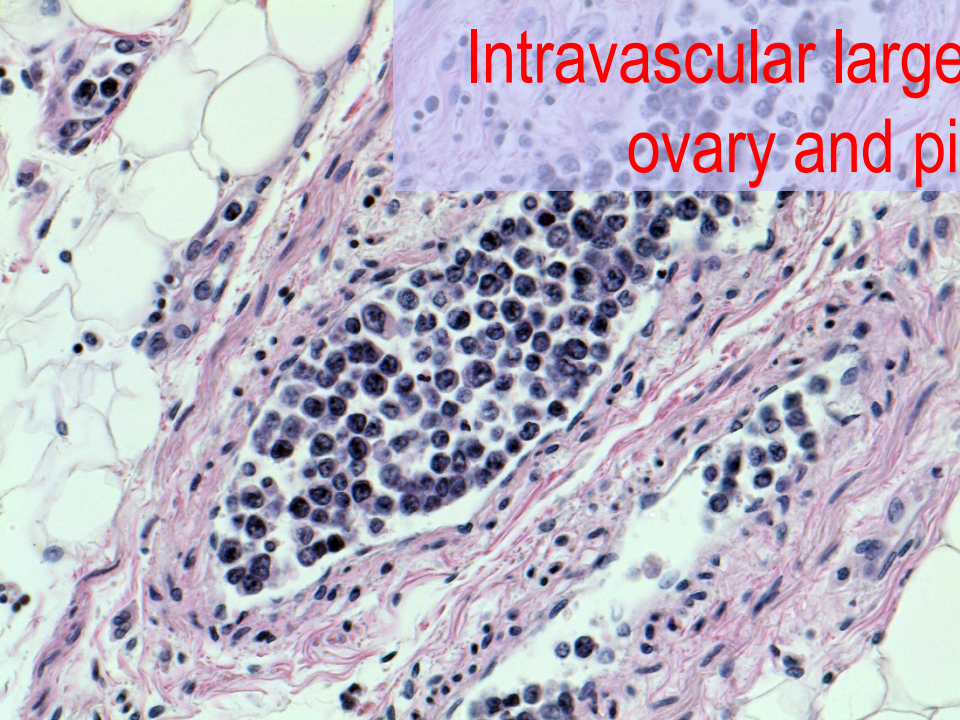
July 10, 20XX



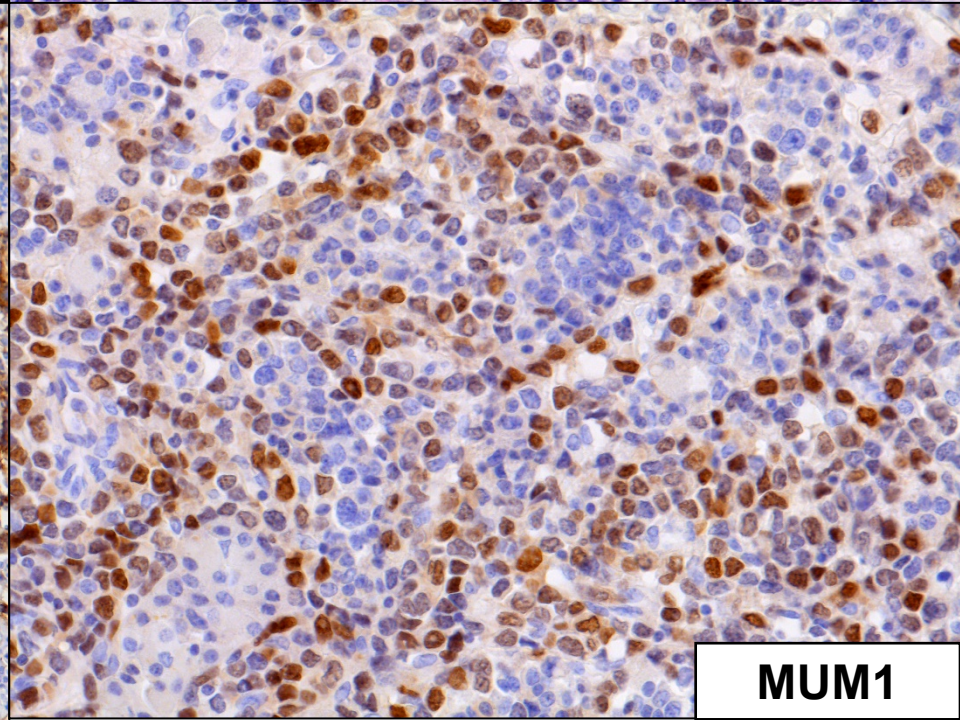
September 12, 20XX



Intravascular large B-cell lymphoma,  
ovary and pituitary gland

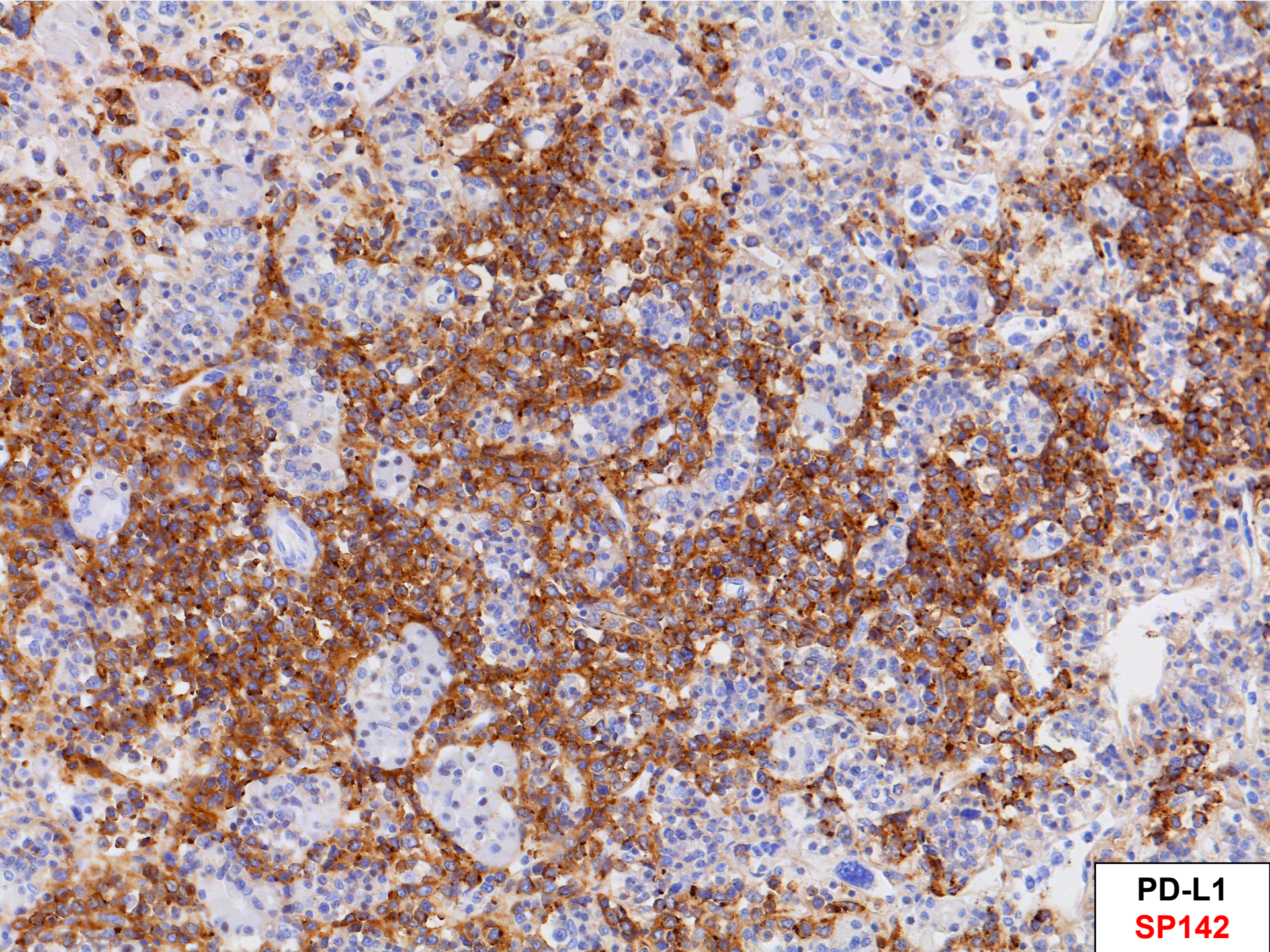


CD20



MUM1





**PD-L1**  
**SP142**





## Expression pattern of IVLBL in each PD-L1 clone

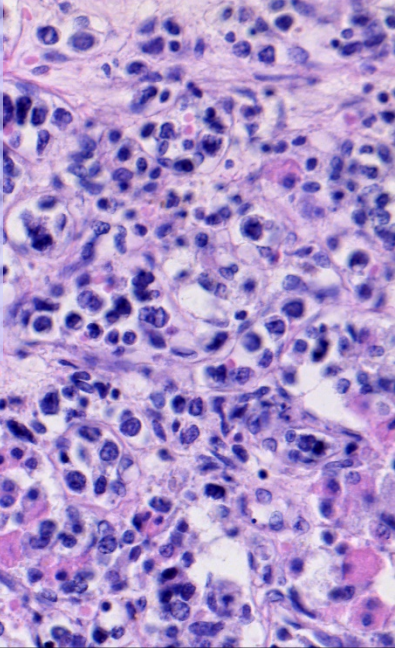
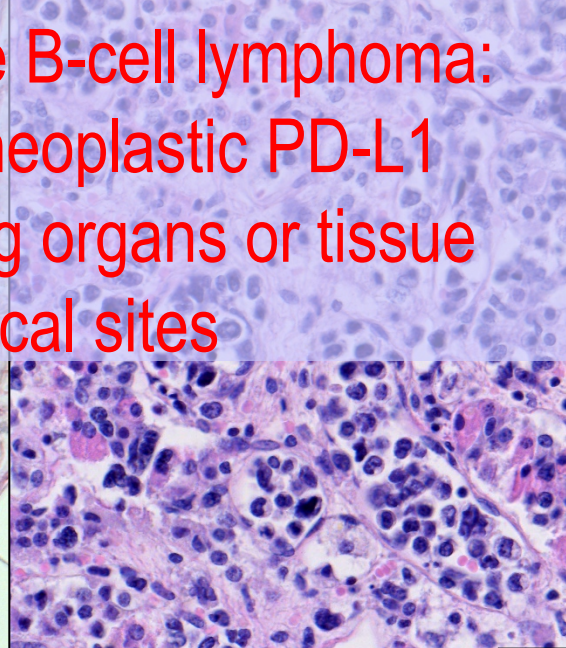
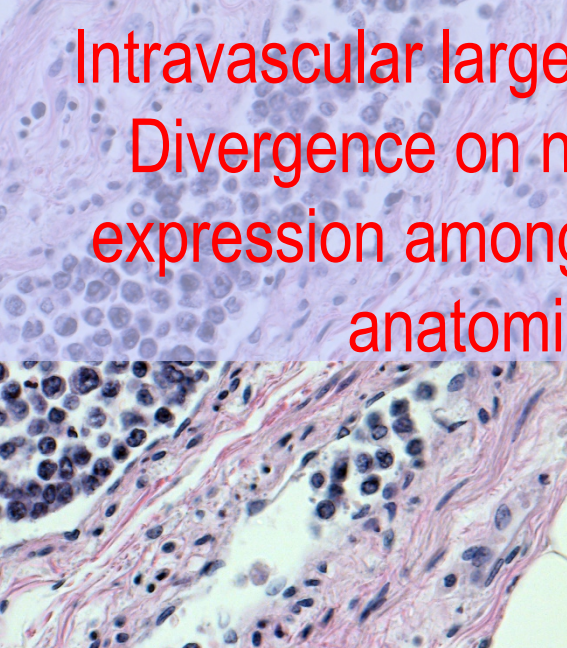
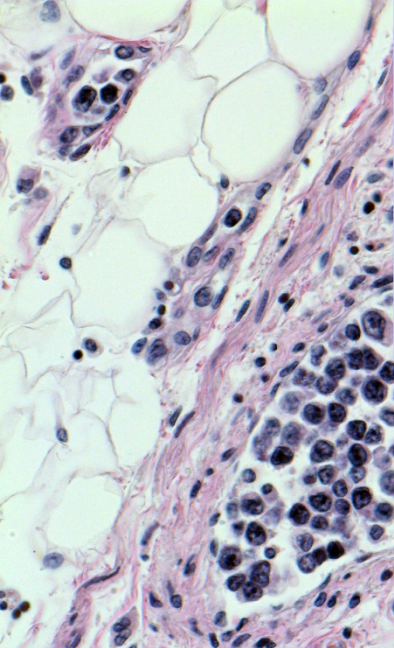
**Table2**

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SP142	+	+	—	+	—	—	+	—	—	+	—	+	—	+	+	—	—
E1J2J	+	+	—	+	—	—	+	ND	+	+	—	+	—	+	+	—	+
28-8	+	+	+	+	+	+	+	ND	+	+	+	+	+	+	+	—	+
	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
SP142	—	—	—	+	+	—	—	—	—	—	—	—	+	—	—	—	+
E1J2J	—	—	—	+	+	—	—	—	—	—	+	+	+	—	—	+	+
28-8	+	+	—	+	+	—	+	—	—	+	+	+	+	—	—	+	+

- The positivity rate of IVLBL cases for SP142, E1J2J and 28-8 clones were 35%, 52% and 79%, respectively
- All of the three clones showed same expression pattern in 19 (58%) of 33 cases examined, while the other 14 (42%) had a heterogeneity among different clones

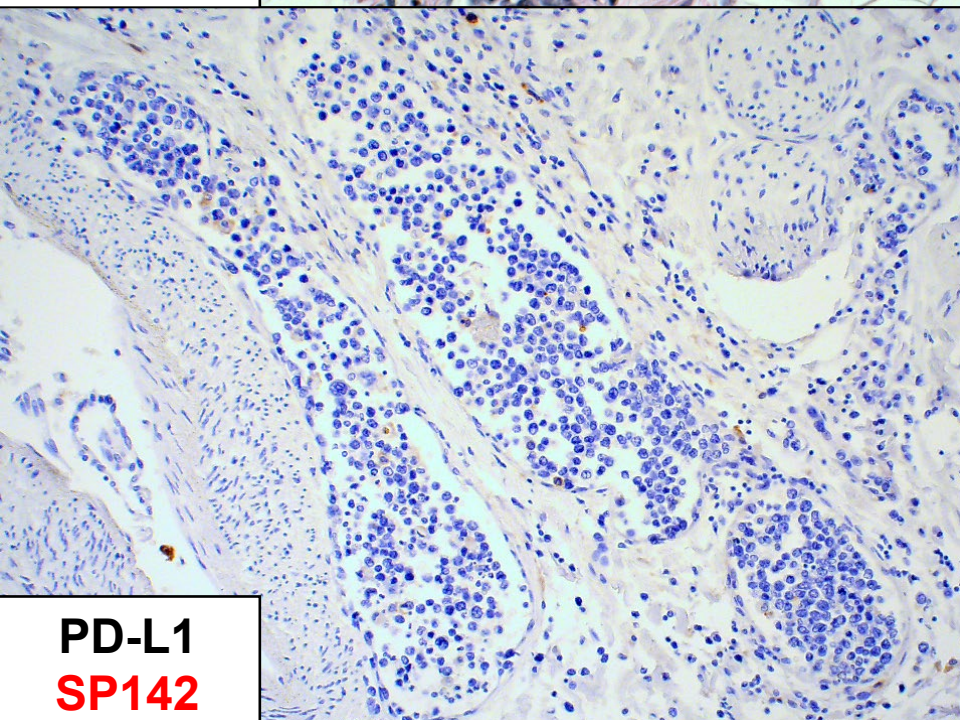


Intravascular large B-cell lymphoma:  
Divergence on neoplastic PD-L1  
expression among organs or tissue  
anatomical sites

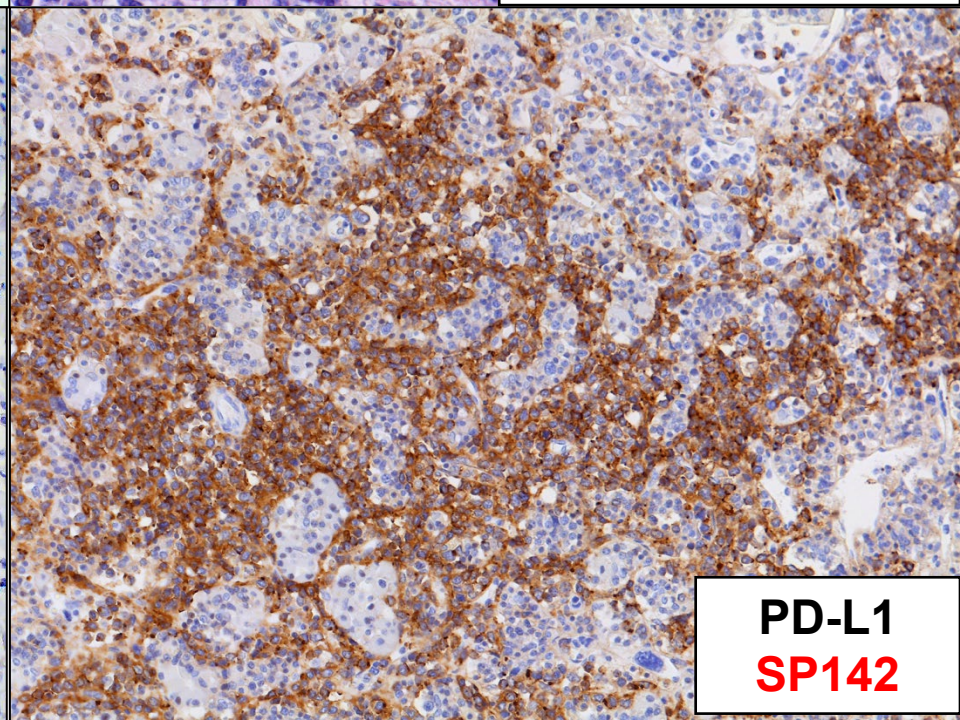


Ovary

Pituitary gland

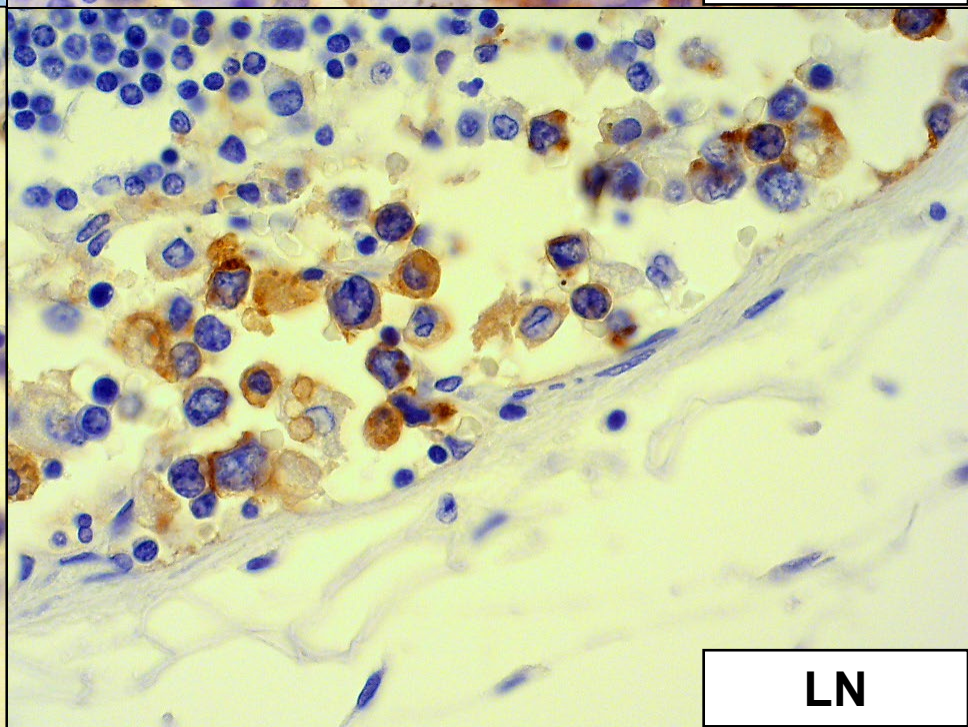
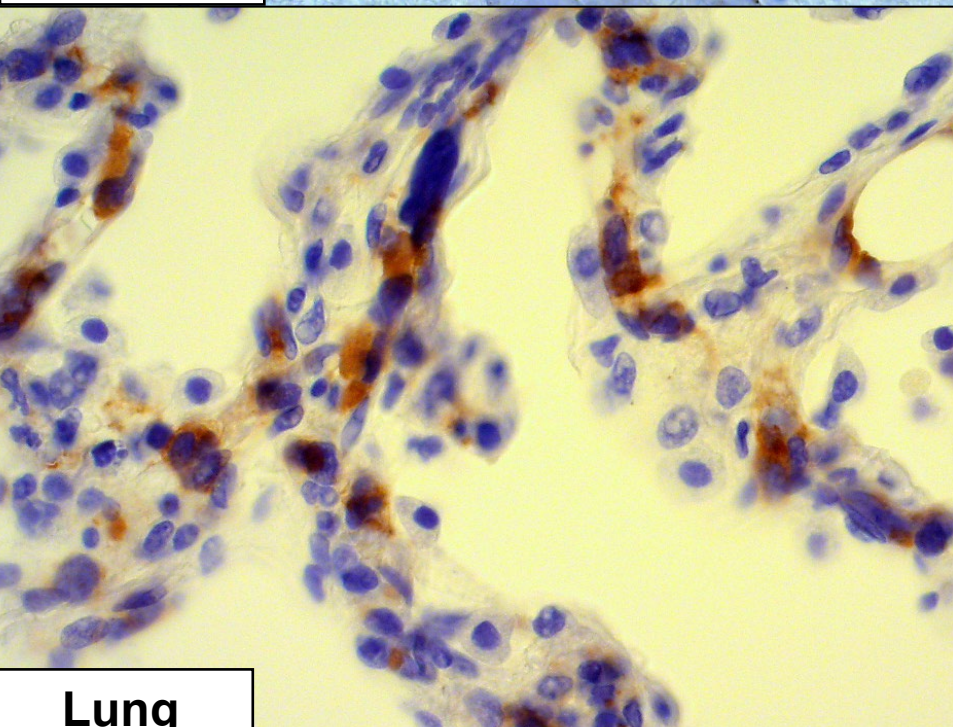
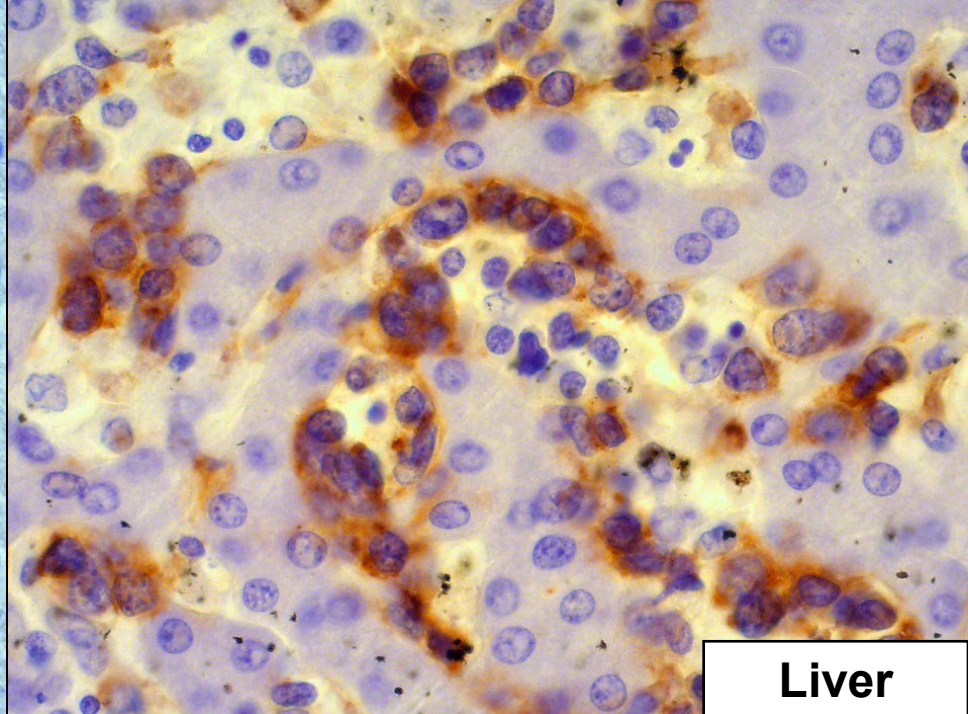


PD-L1  
SP142

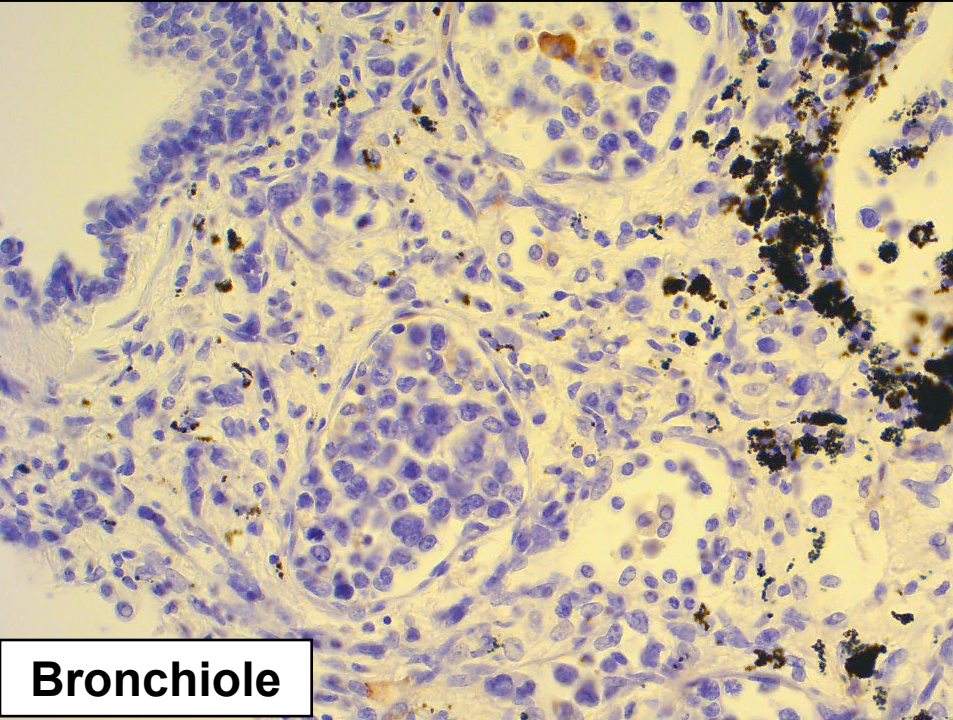


PD-L1  
SP142

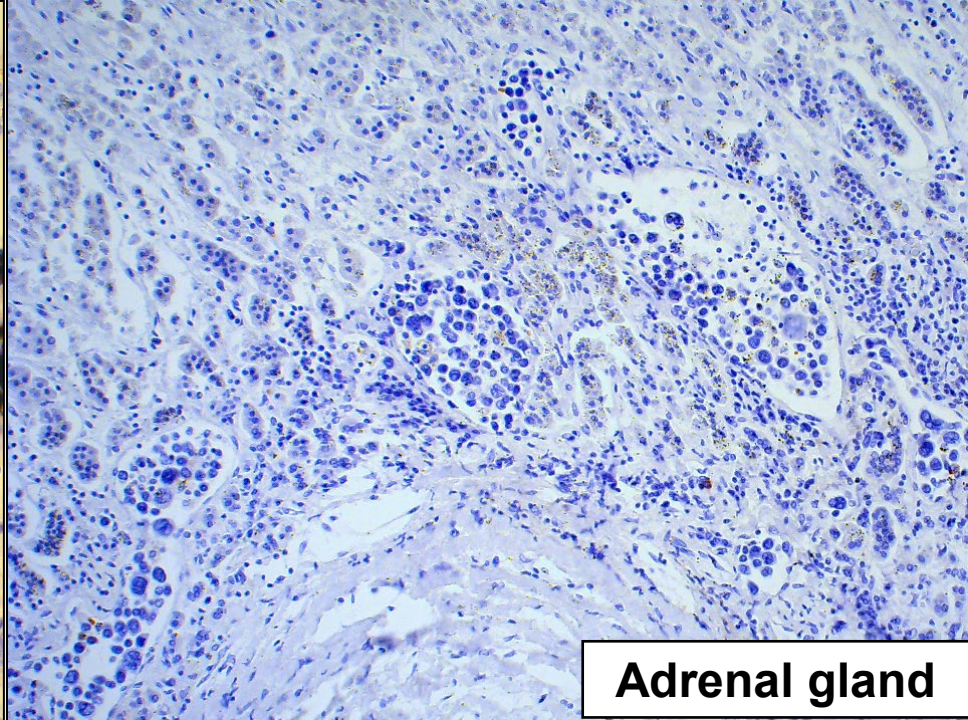




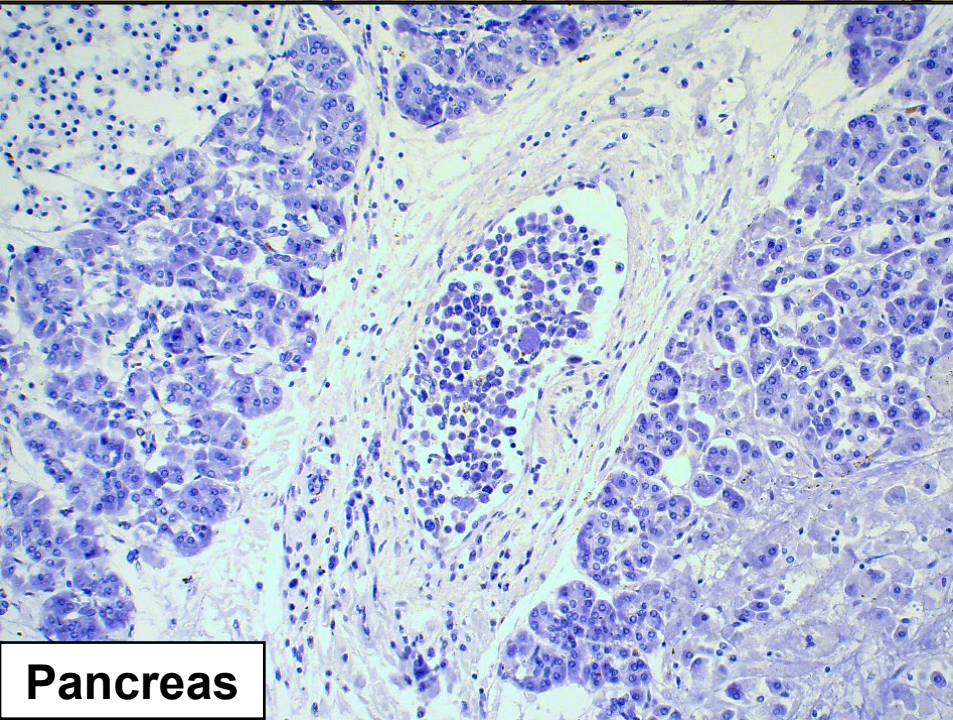




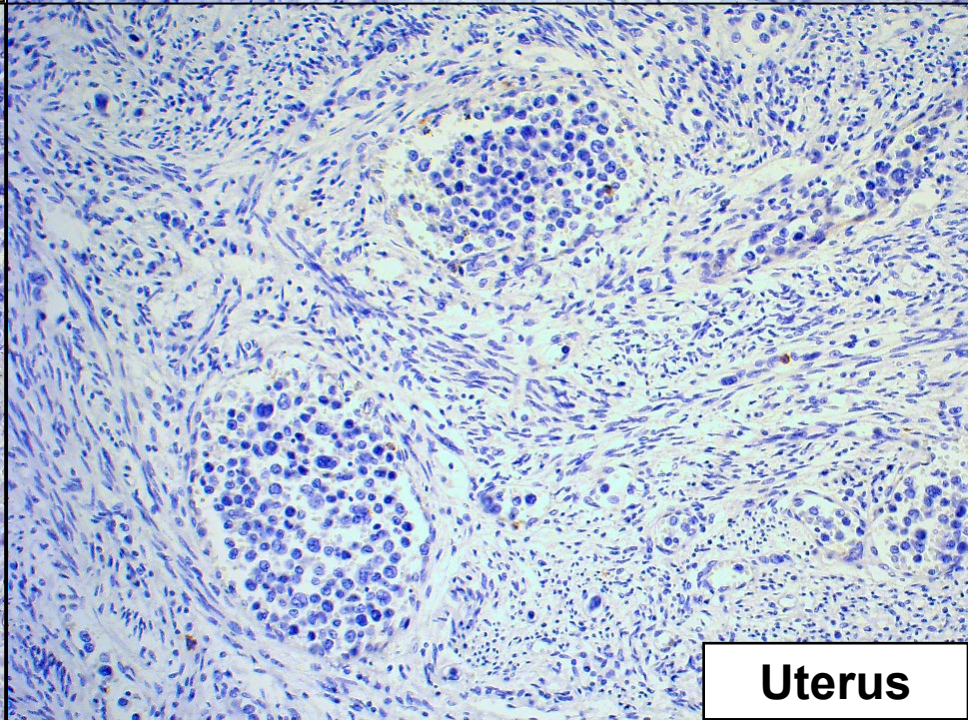
**Bronchiole**



**Adrenal gland**

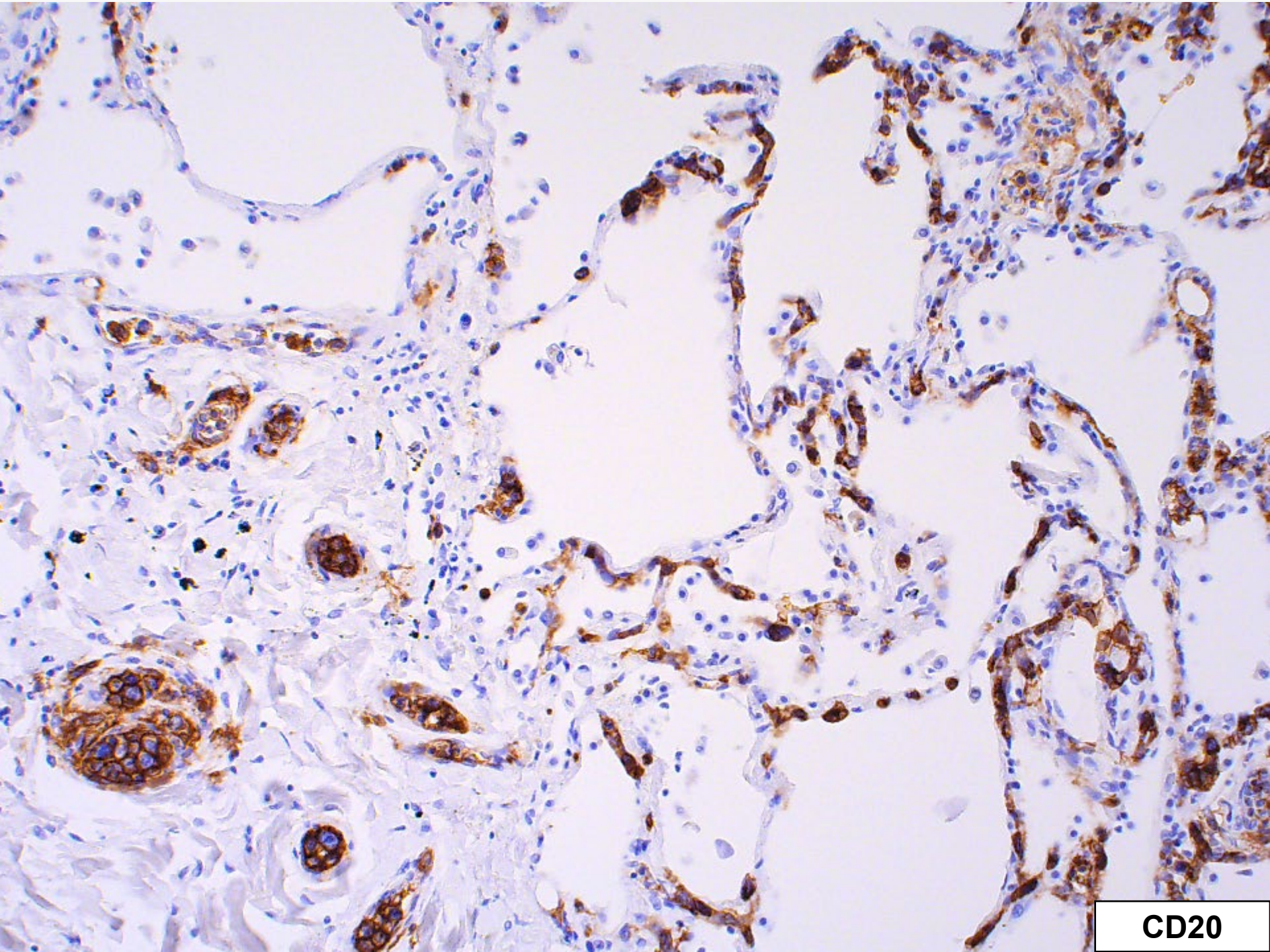


**Pancreas**



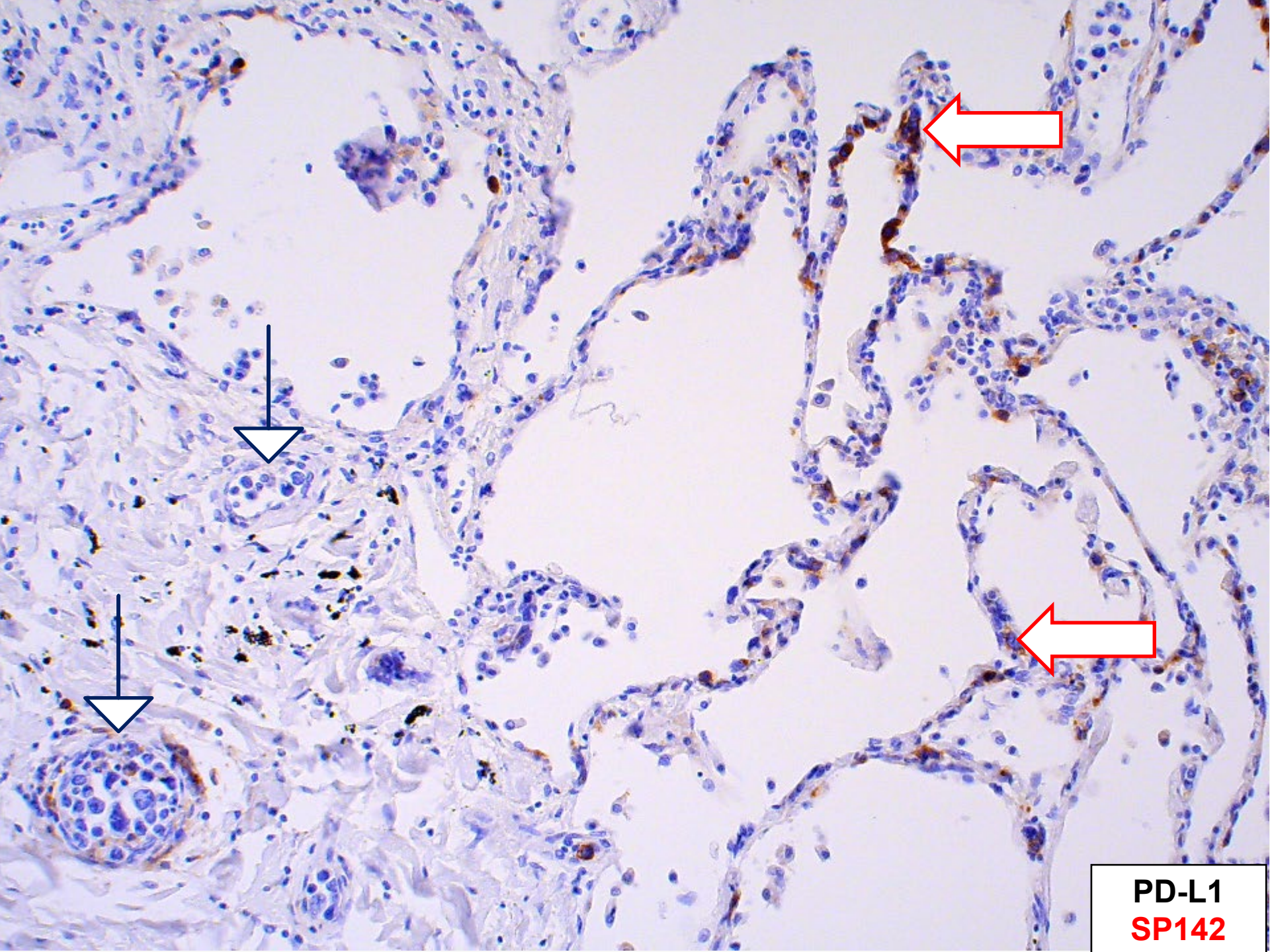
**Uterus**





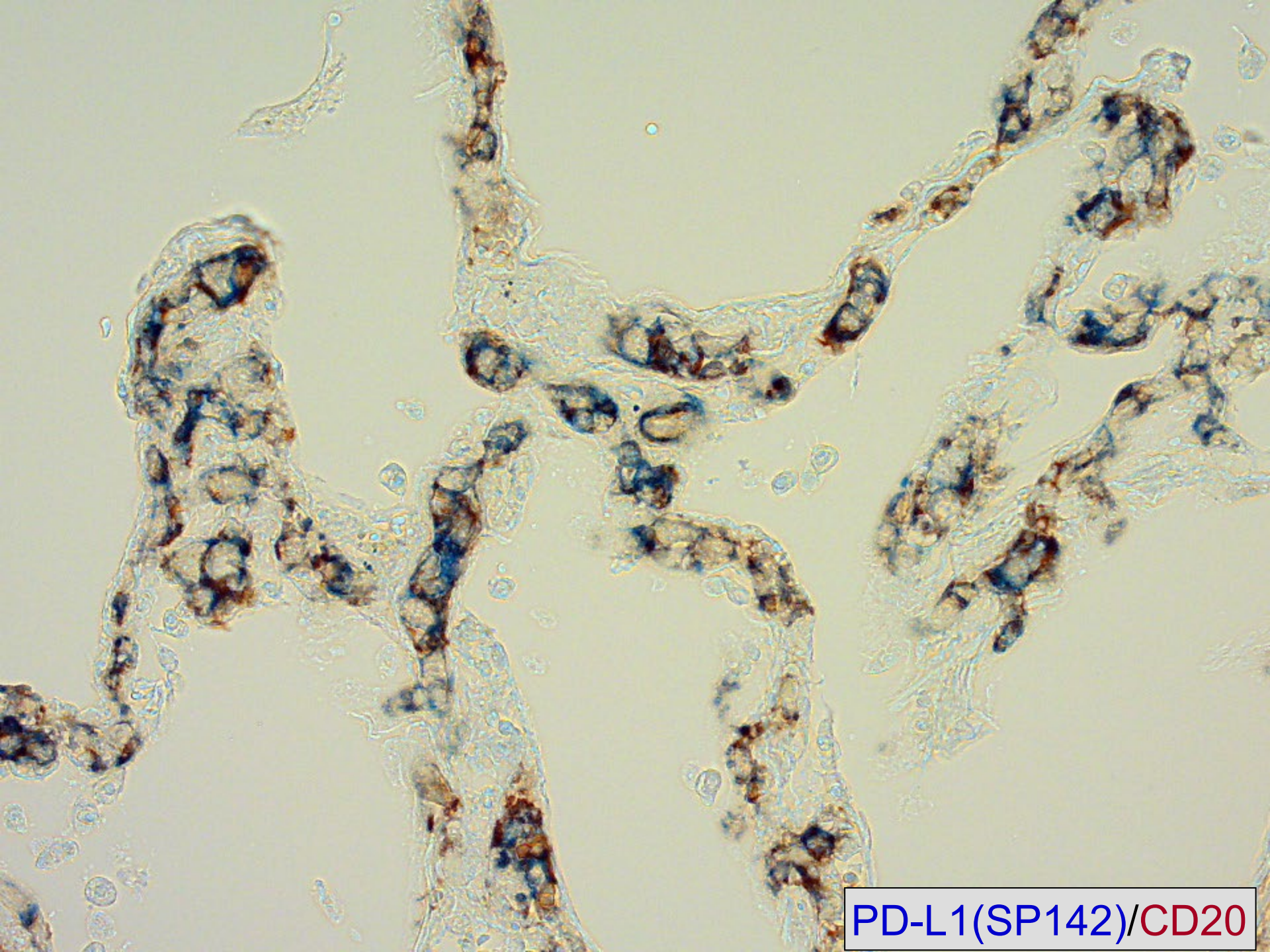
CD20





**PD-L1**  
**SP142**





PD-L1(SP142)/CD20



# IVLBCL: Divergence on neoplastic PD-L1 expression among organs and tissue anatomical sites

## Neoplastic PD-L1+

- Pituitary gland
- CNS
- Liver
- Spleen
- BM
  - Diffuse extra-sinusoidal invasion
- LN
  - Sinuses
- Lung
  - Capillaries

## Neoplastic PD-L1-negative

- Adrenal gland
- Thyroid gland
- Pancreas
- Ovaries
- Uterus
- Pleura
- Lung
  - Bronchiole vessels

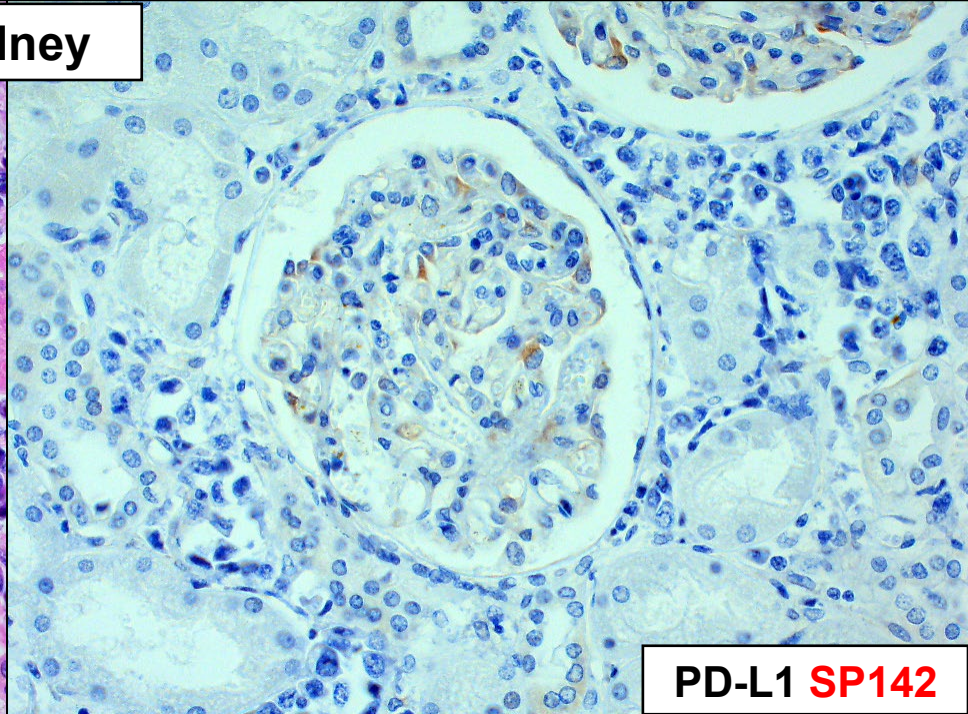
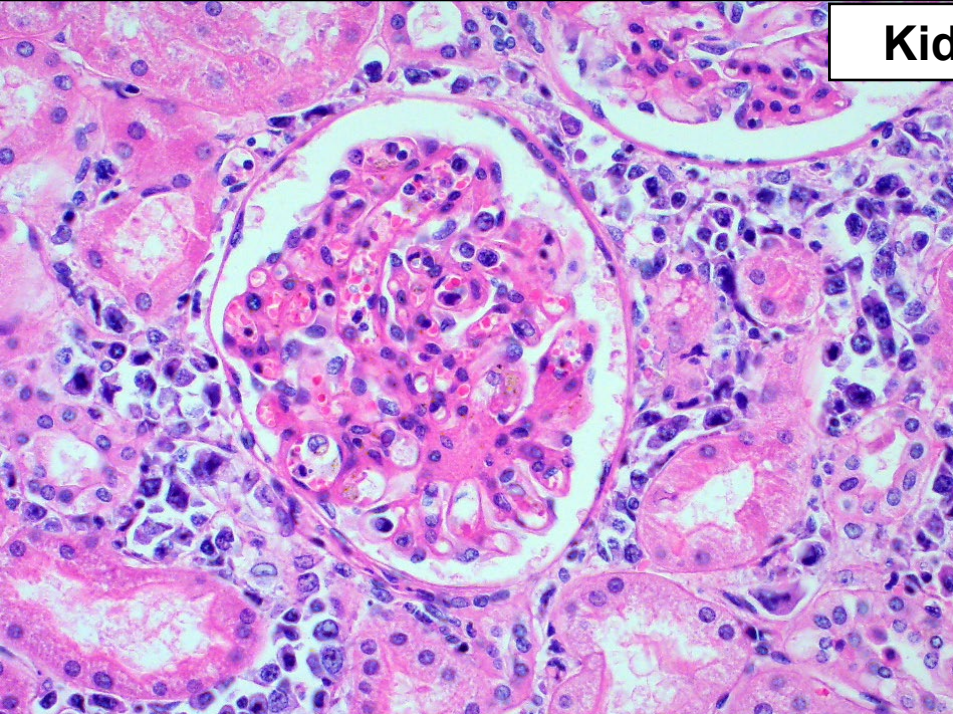


# Heterogeneity on neoplastic PD-L1 expression among IVLBCL autopsy cases

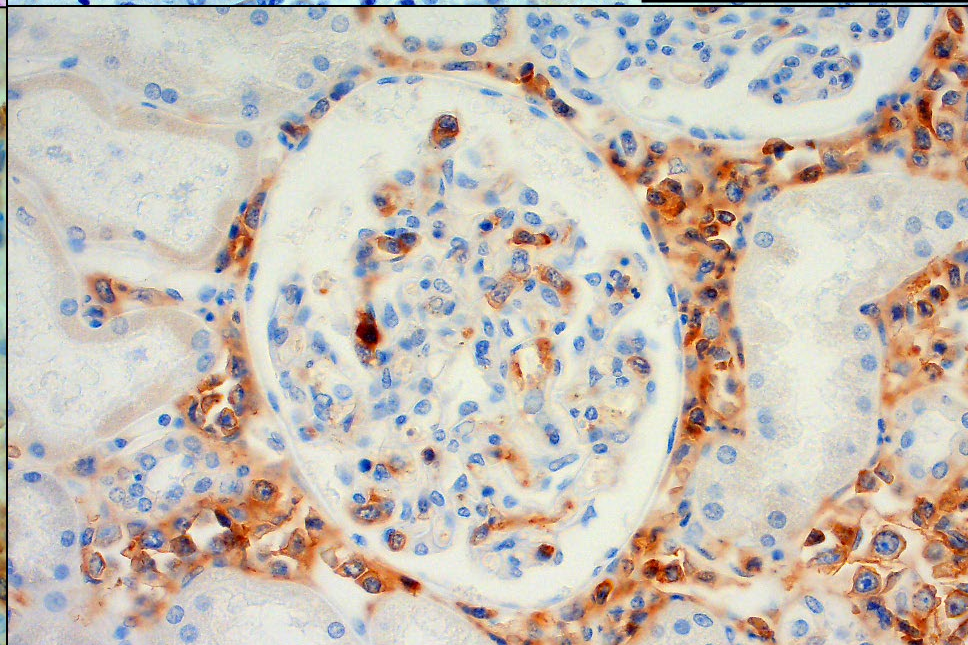
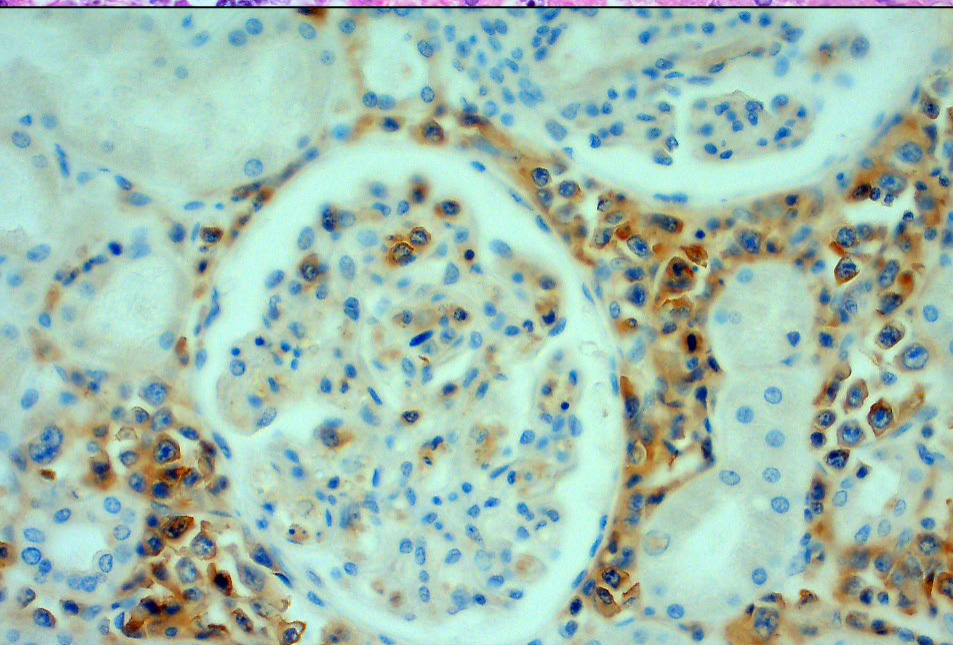
- IVLBCL 剖検例 10症例(M:F=5:5)
- 年齢中間値 61歳 (51～99歳)
- 2例で腫瘍細胞がPD-L1陽性
- 1例はPD-L1抗体3クローン(SP142, 28-8, E1J2J)全てに陽性。しかし臓器間、また同一臓器でも組織学的な解剖学的部位の差異によりPD-L1発現に明らかな多寡を示した
- 他の1例は、2クローン(28-8, E1J2J)に陽性、1クローン(SP142)に陰性、臓器・組織学的部位のいずれでも陽性
- 残り8例は全く陽性所見なし、ホルマリン過固定？



**Kidney**



**PD-L1 SP142**



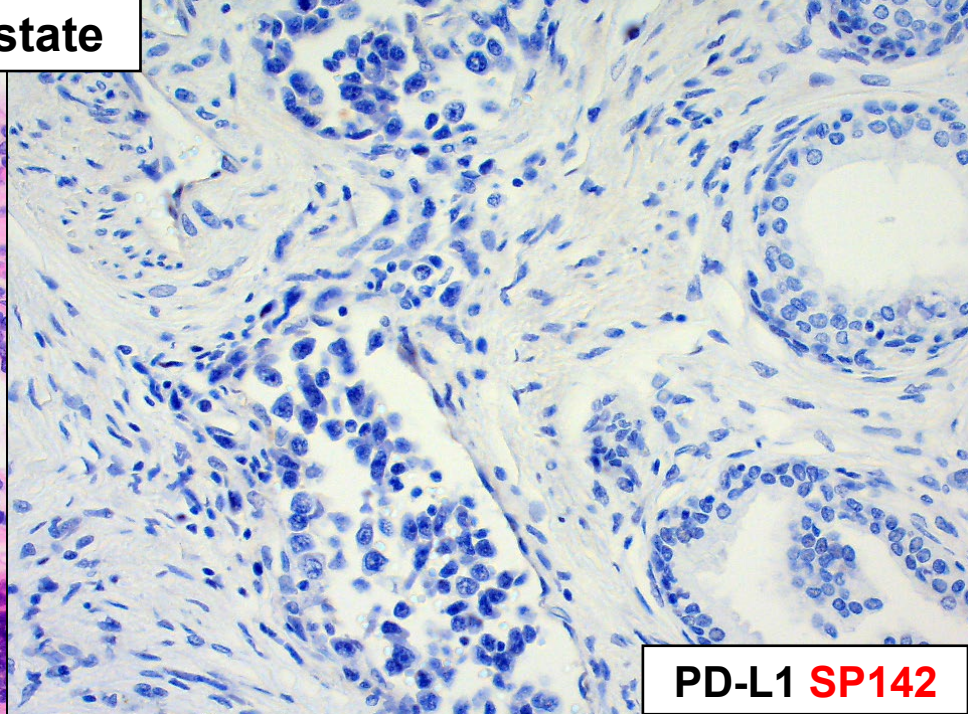
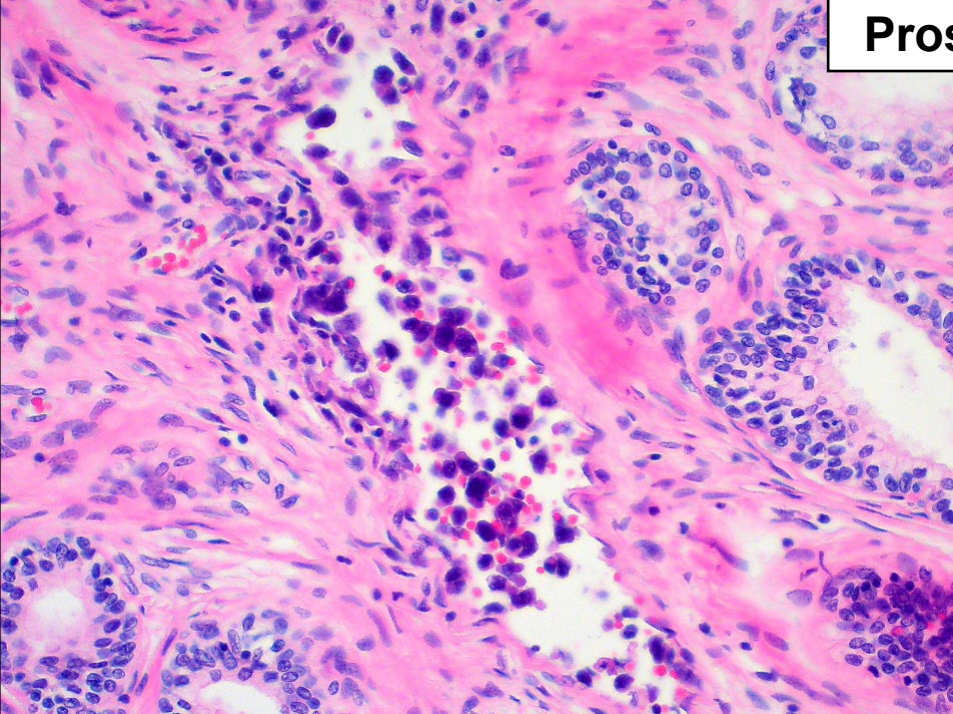
**PD-L1 28-8**

**Case #7, 57 yrs old M, Autopsy**

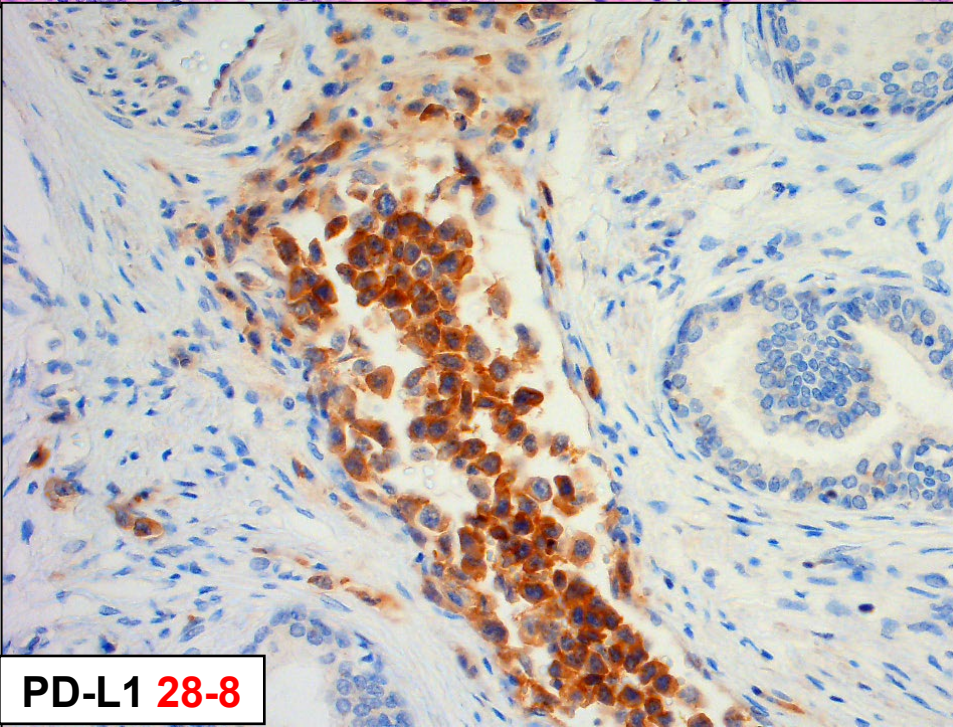
**PD-L1 E1J2J**



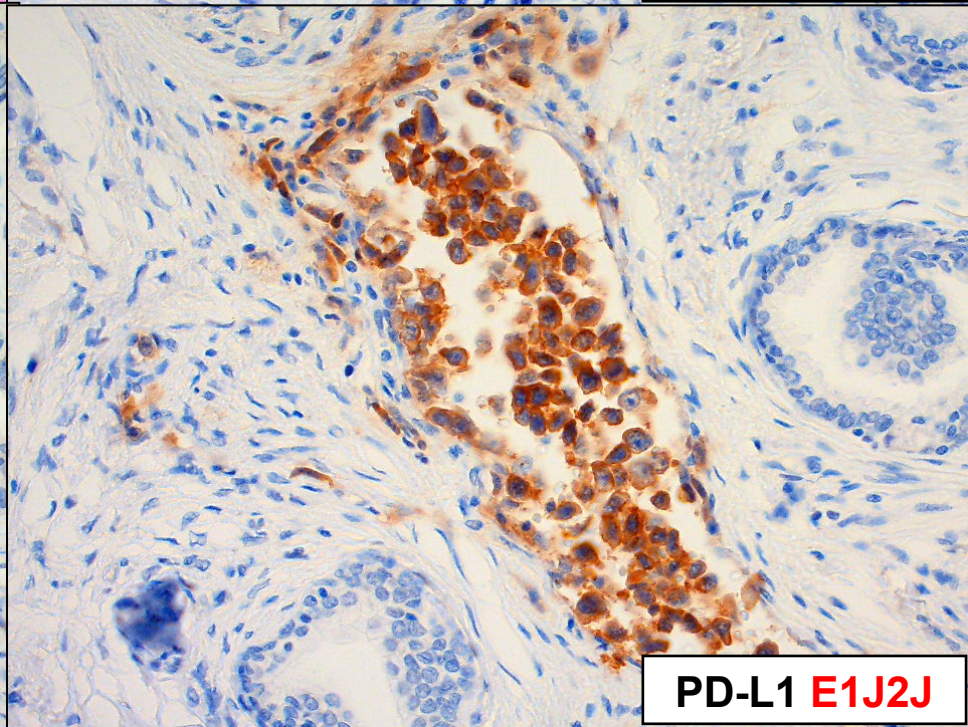
**Prostate**



**PD-L1 SP142**



**PD-L1 28-8**



**PD-L1 E1J2J**



# IVLBCL: Heterogeneity on neoplastic PD-L1 expression among autopsy cases

## Case #1

- Tumor cells are positive for all three antibodies (SP142, 28-8 and E1J2)
- Divergence in expression pattern dependent on the localization of the tumor cells in organs and tissue anatomical sites

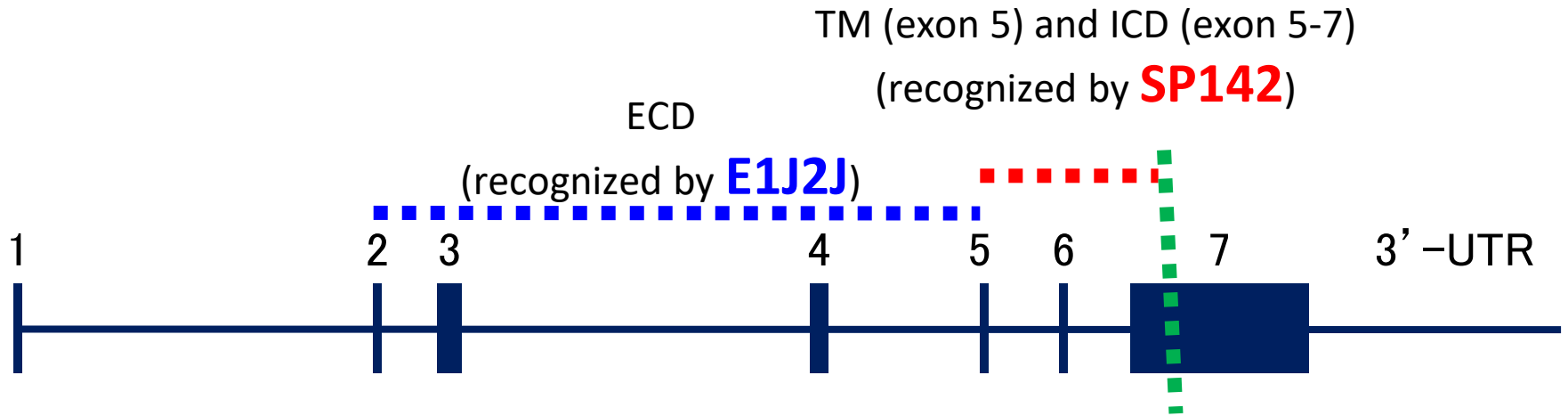
## Case #2

- Tumor cells are positive for 28-8 and E1J2, but not SP142
- Universally positive without any divergence beyond the affected anatomical sites

Aberrant PD-L1 expression through 3'-UTR disruption  
Kataoka, Nature 2016



# PD-L1



ECD: Extracellular Domain; TM: Transmembrane Domain; ICD; Intracellular domain

Exon 1 : 5450542-5450597 (hg19)

Exon 2 : 5456100-5456166

Exon 3 : 5457079-5457421

Exon 4 : 5462834-5463121

Exon 5 : 5465499-5465606

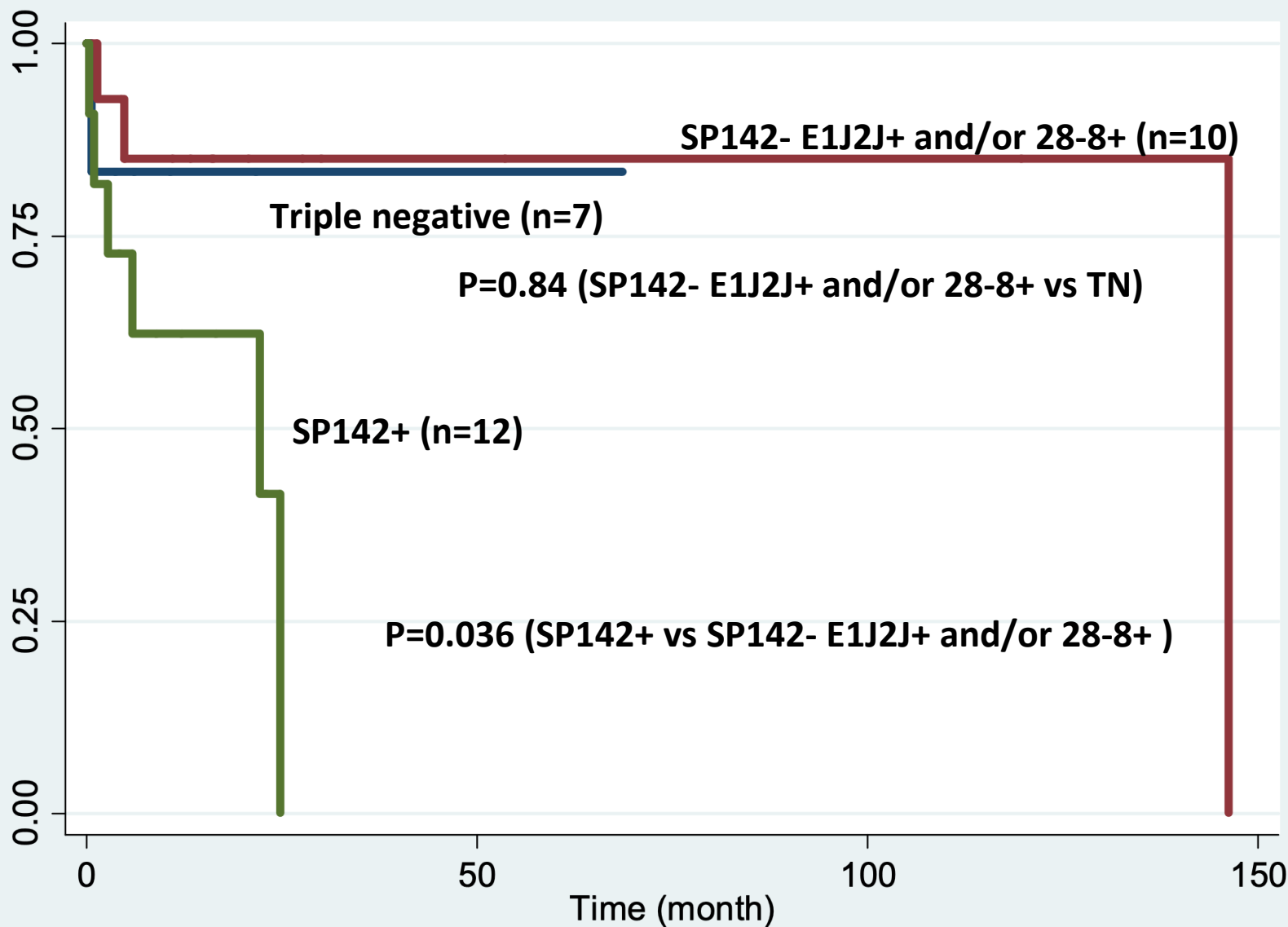
Exon 6 : 5466770-5466829

Exon 7 : 5467840-5470554



Survival curves of patients treated with R-based chemotherapy, according to PD-L1 expression (*Satou A et al in preparation*)

OS



# Clinical features of PD-L1(SP142)-positive IVLBL

Table 1 Comparison between PD-L1(SP142)-positive and –negative IVLBL

Variables	PD-L1 <sup>+</sup> IVL (n=12)	PD-L1 <sup>-</sup> IVL (n=22)	p
Sex (Male/Female)	5/7	11/11	0.72
Age, median (range),	74 (51-81)	75 (64-86)	0.036
Age, average	69	76	
Age>60years	9/12 (75%)	22/22 (100%)	0.037
Performance status>1	8/12 (75%)	16/21 (76%)	0.69
IPI (HI/H)	10/11 (91%)	20/21 (95%)	1.0
plt < 14x10 <sup>4</sup> /μl	9/11 (82%)	14/21 (67%)	0.44
WBC < 3.5x10 <sup>3</sup> /μl	4/11 (36%)	3/21 (14%)	0.20
Hb < 11.0	9/11 (81%)	15/21 (71%)	0.68
Alb < 3.0g/dl	8/11 (73%)	19/21 (90)	0.31

- PD-L1<sup>+</sup> IVLBL showed significantly lower age distribution (P=0.036) and lower frequency of patients older than 60 years (P=0.037).



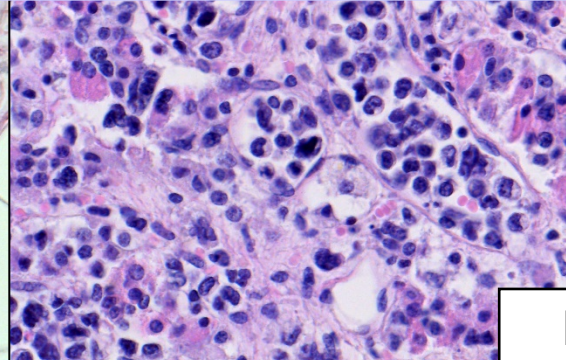
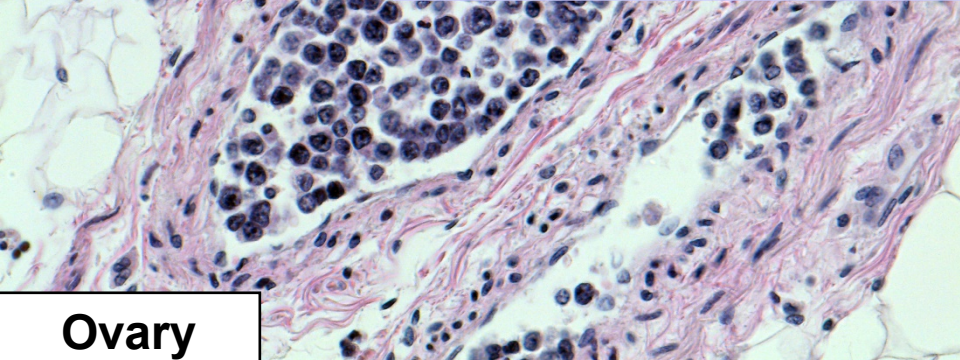
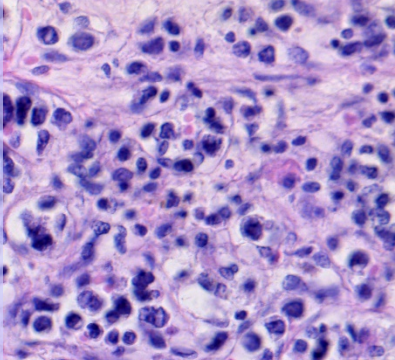
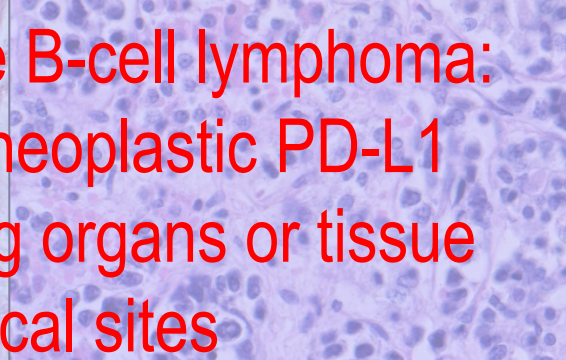
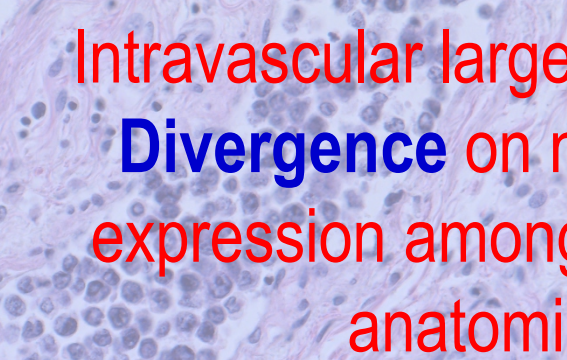
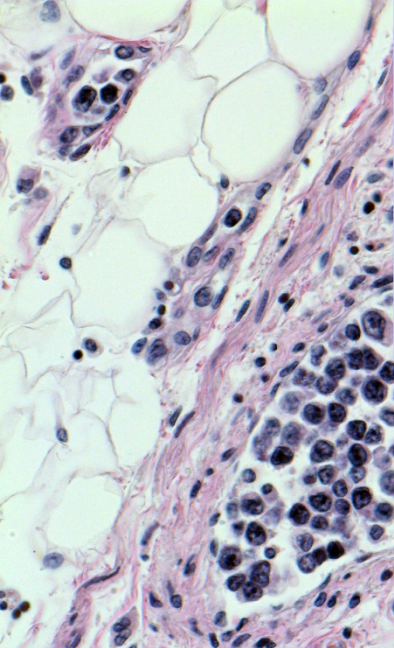
**Table 1 Continued**

<b>Variables</b>	<b>PD-L1<sup>+</sup> IVL (n=12)</b>	<b>PD-L1<sup>-</sup> IVL (n=22)</b>	<b>p</b>
<b>B symptoms</b>	<b>8/12 (67%)</b>	<b>19/22 (86%)</b>	<b>0.21</b>
<b>Hepatomegaly</b>	<b>1/12 (8.3%)</b>	<b>4/19 (21%)</b>	<b>0.62</b>
<b>Splenomegaly</b>	<b>7/12 (58%)</b>	<b>8/19 (42%)</b>	<b>0.47</b>
<b>Respiratory symptoms</b>	<b>1/12 ( 8%)</b>	<b>10/18 (56%)</b>	<b>0.018</b>
<b>CNS symptoms</b>	<b>6/12 (50%)</b>	<b>8/19 (42%)</b>	<b>0.72</b>
<b>Variant (Classic/HPS)</b>	<b>2/9</b>	<b>1/20</b>	<b>0.27</b>
<b>CD5 positivity</b>	<b>2/7 (29%)</b>	<b>8/19 (42%)</b>	<b>0.67</b>
<b>Hans (GCB/non-GCB)</b>	<b>1/6</b>	<b>2/15</b>	<b>1.0</b>

- PD-L1<sup>+</sup> IVLBL had respiratory symptoms significantly less frequently than PD-L1<sup>-</sup> group.



Intravascular large B-cell lymphoma:  
**Divergence** on neoplastic PD-L1  
expression among organs or tissue  
anatomical sites



Ovary

Pituitary gland

Suppression ?

Activation ?

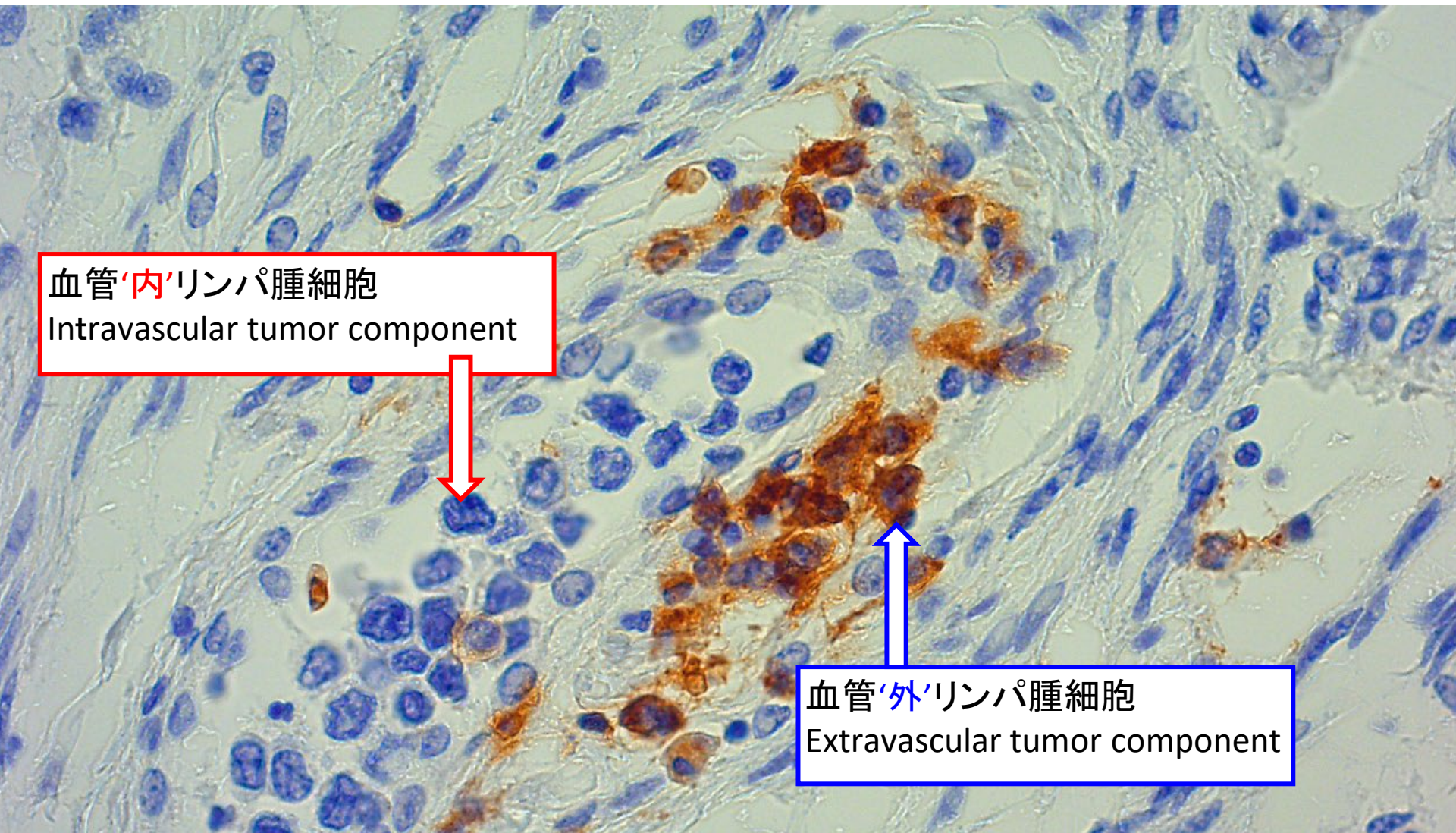
PD-L1  
SP142

Case #6, 51 yrs F, autopsy

PD-L1  
SP142



血管内大細胞型B細胞リンパ腫 Intravascular Large B-cell Lymphoma  
Suppression or activation of PD-L1 expression on lymphoma cells?



PD-L1免疫染色 (SP142抗体)  
PD-L1 immunostain (clone SP142)

# PD-L1 and CD80/B7.1 regulate angiogenesis

(*Am J Pathol* 2011;178:1922)

*Vascular Biology, Atherosclerosis, and Endothelium Biology*

A Novel Function for Programmed Death Ligand-1

*Regulation of Angiogenesis*

- PD-L1 and its receptor CD80, but not PD-1, are expressed by primary murine lung and heart vascular endothelial cells and the microvascular endothelial cell line (MS1) at both the mRNA and protein levels *in vitro*.
- The expression of PD-L1 in both vascular endothelial cells and corneal epithelial cells regulates corneal angiogenesis.



# Neoplastic PD-L1 Expression on DLBCLs

(Suzuki Y et al. Pathol Int 2019)

- 悪性リンパ腫 528例、2015年から2017年、うちDLBCLは283例
- 抗PD-L1抗体 (SP142 clone) でスクリーニング、必要に応じて28-8 および E1J2J clone を使用
- EBV+ DLBCL-NOS、8例中4例が **neoplastic** PD-L1陽性
- さらに節外性DLBCL (EBV陰性) 108例中、6例(5.5%)が **neoplastic** PD-L1陽性
- 一方、本コホートにおける中枢神経原発 (15例)、睾丸原発 (5例)、あるいは皮膚原発下肢型 DLBCL (2例) にPD-L1陽性例は見出されなかった

# Neoplastic PD-L1+ Extranodal DLBCLs

- 6例、発症年齢中間値 71歳 (51～74歳) 、男女比 2 : 4
- 剖検 (n=1)、皮膚 (n=1)、副腎 (n=1)、副腎と骨髄 (n=1)、骨盤腔内腫瘍 (n=1)、腎臓 (n=1)
- 血管内大細胞型B細胞リンパ腫 2例、DLBCL-NOS 4例、うち 3例に血管内増殖パターン、また de novo CD5+ DLBCLを 1例含む
- Neoplastic PD-L1陽性率 腫瘍細胞の 10 から >90%
- 免疫組織学的表現型 : CD3-, CD20+, BCL-2+, MUM1+, CD5あるいはCD10陽性は各 1例、BCL6陽性は 4例



## Primary Intestinal DLBCL: Pathology (*Ishikawa E, et al. Cancer Med 2018*)

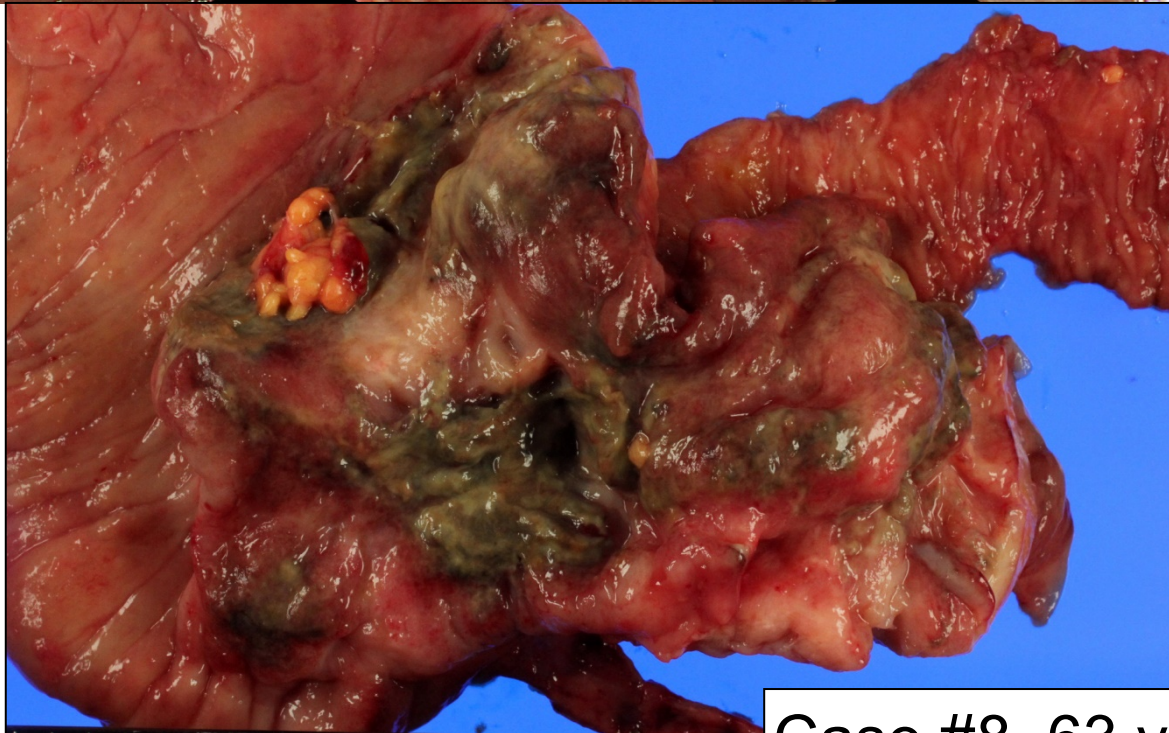
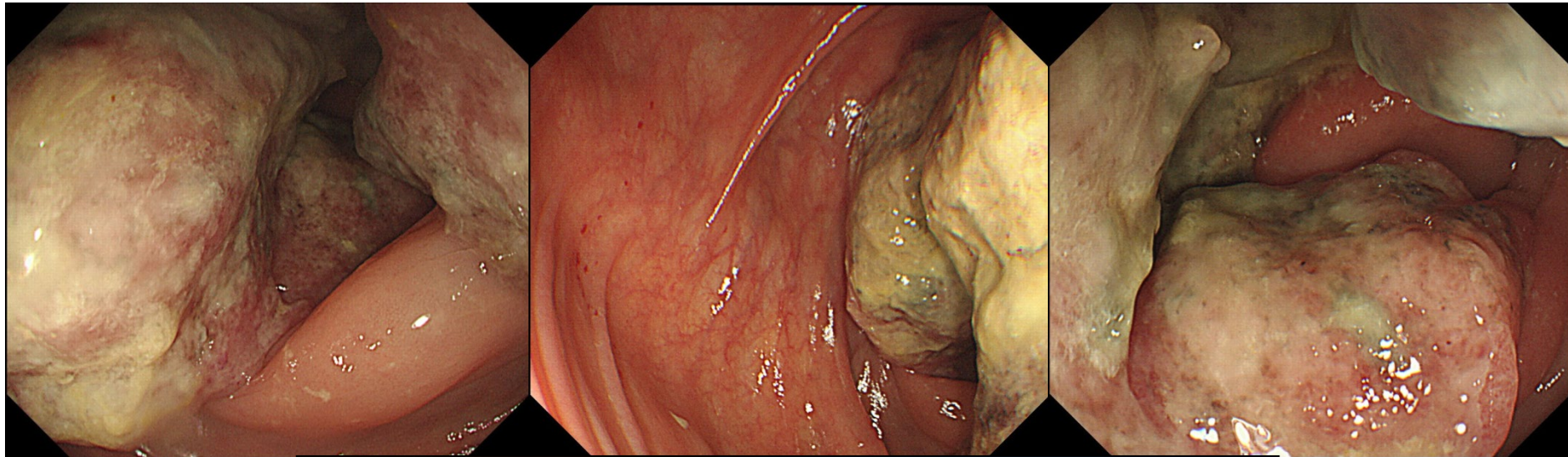
- EBV+ DLBCL 62 patient with primary intestinal DLBCL diagnosed between 2004 and 2017
- 42 males and 20 females with a median age of 68 years (range 15-88 years)
- 51 patients received rituximab-containing chemotherapy
- Anatomical sites: duodenum (n=5), jejunum (n=13), ileum (n=8), ileocecum (n=22), colon (n=5), rectum (n=5), and multiple sites (n=4)

# Primary Intestinal DLBCL: Pathology

- DLBCL with neoplastic PD-L1 expression, but no EBV association (**n=1**)
- EBV+ DLBCL (n=10, 16%)
  - Two with neoplastic PD-L1 expression
  - Treated lymphoma-associated (n=4)
  - Iatrogenic immunodeficiency-associated (n=3)
  - One with synchronous gastric carcinoma
- *De novo* CD5+ DLBCL (n=4)
- DLBCL, NOS, without any of CD5 positivity, neoplastic PD-L1 expression, or EBV (n=47)



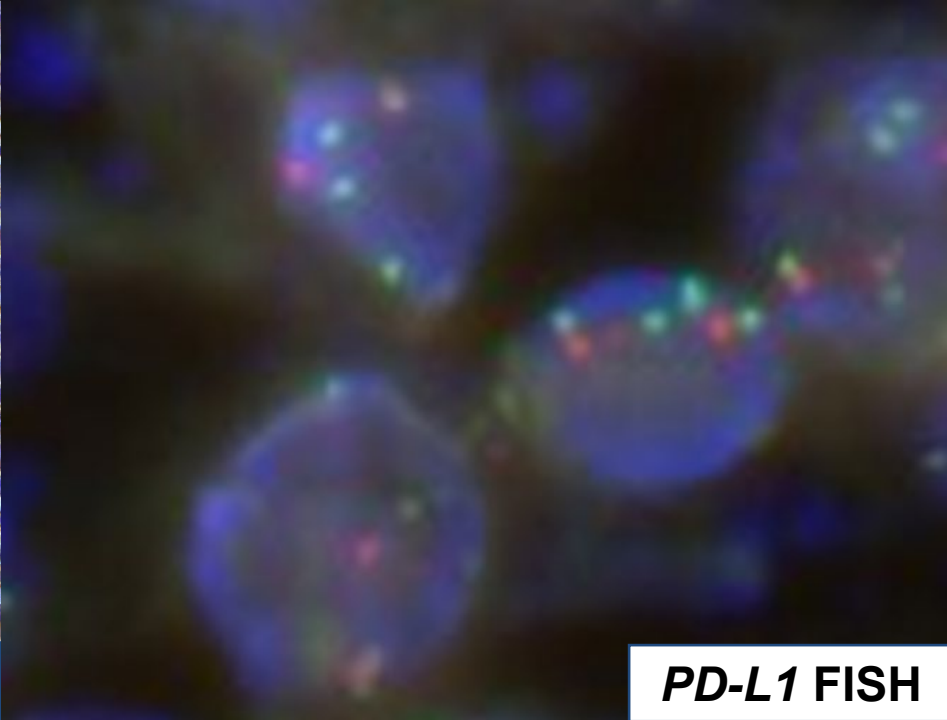
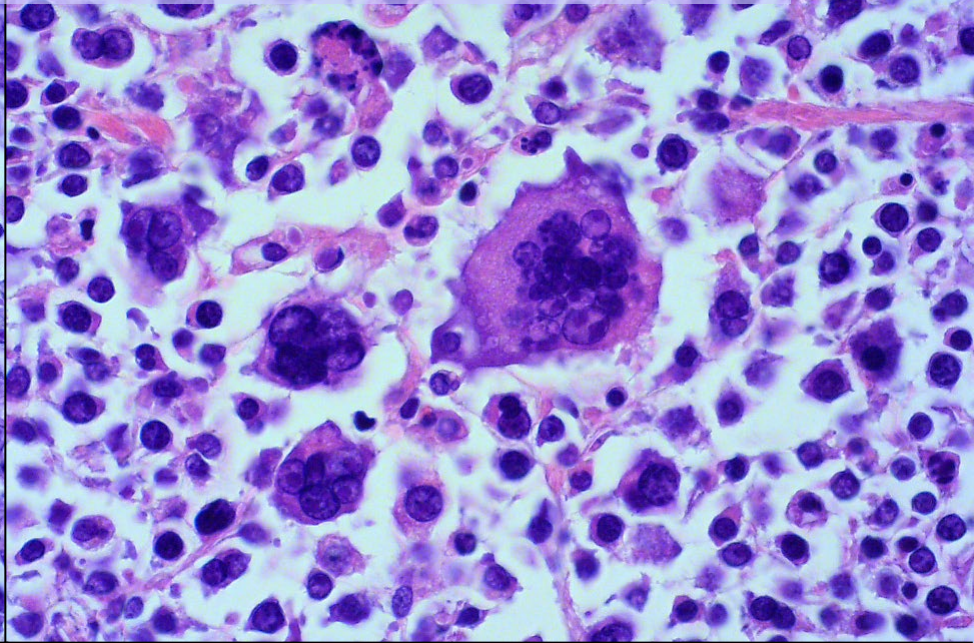
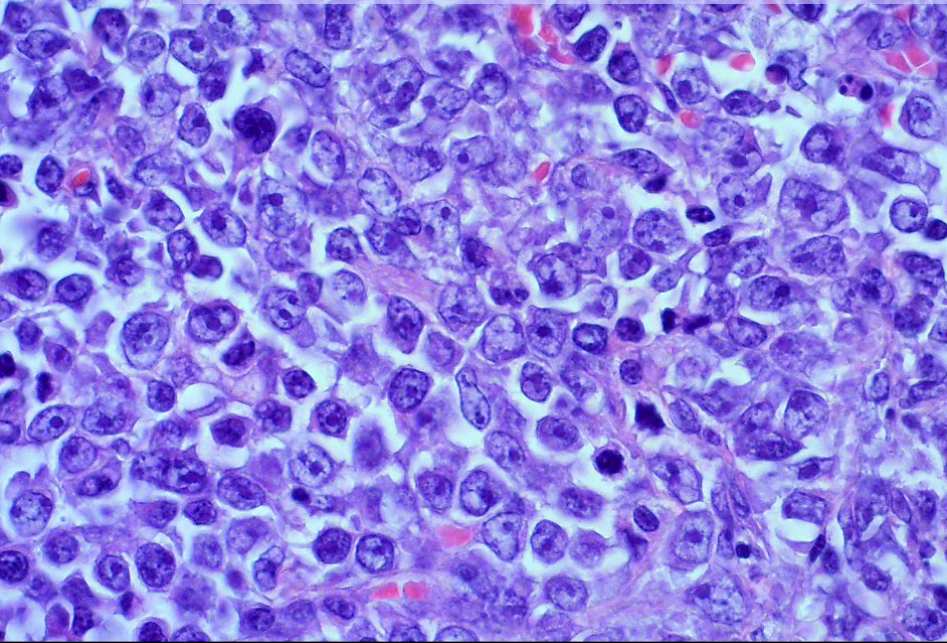
Primary intestinal DLBCL with neoplastic PD-L1 expression: Cae #1 63yr M



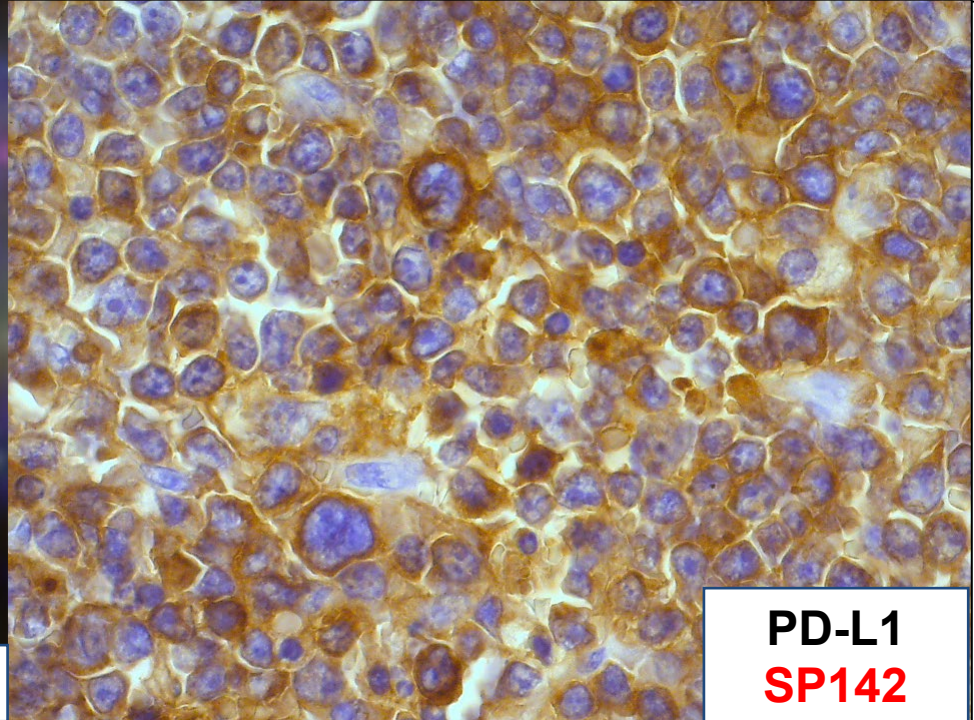
Case #8, 63 yrs M, cecum



Primary intestinal DLBCL with neoplastic PD-L1 expression: Case #1 63yr M



**PD-L1 FISH**



**PD-L1  
SP142**



# Patients with EBV<sup>+</sup>, CD5<sup>+</sup>, or nPD-L1<sup>+</sup> iDLBCL

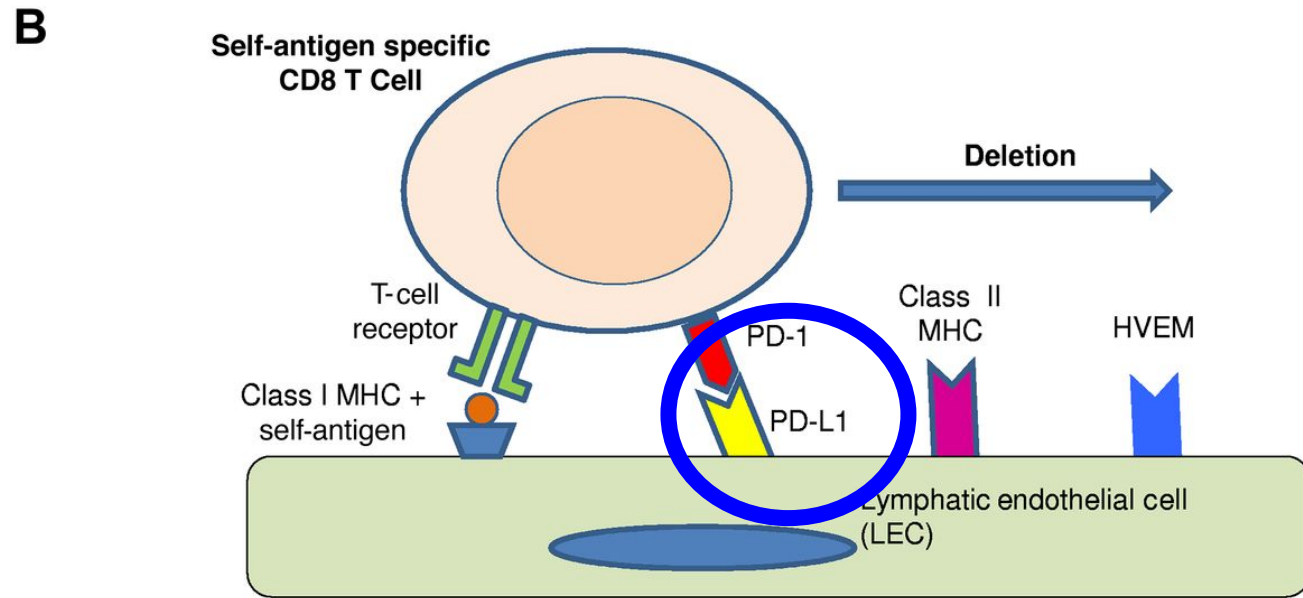
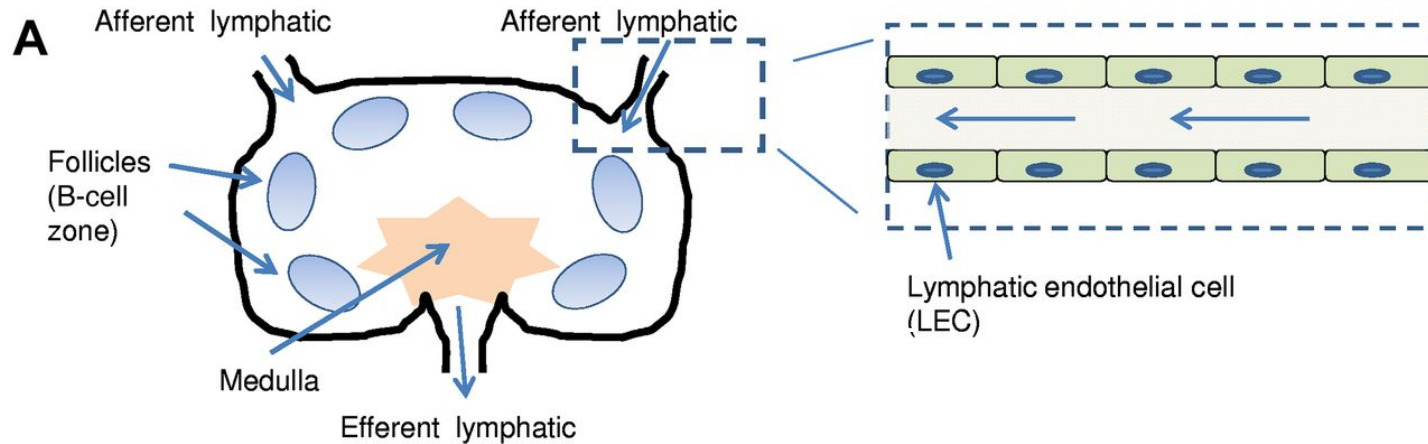
Age	Sex	Primary site	Immuno-suppression	EBV	CD5	nPD-L1	Treatment	Response	Time to Relapse	Status
63	M	Ileocecum	Old age	-	-	<b>+(100%)</b>	R-CTx + Surgery	CR	<b>5</b>	<b>DD</b>
75	F	A colon	Old age	<b>+</b>	-	<b>+(50%)</b>	R-CTx	PR	6	DD
74	F	Ileocecum	<b>PTCL</b>	<b>+</b>	-	<b>+(20%)</b>	R-CTx + Surgery	CR	22	DD
70	F	Ileocecum	<b>PTCL</b>	<b>+</b>	-	-	R-CTx	CR	11	DD
82	F	Duodenum	<b>cHL</b>	<b>+</b>	-	-	No treatment			DOC
80	M	Jejunum	<b>cHL</b>	<b>+</b>	+	-	R-CTx + Surgery	PD		DD
82	F	Ileocecum	<b>MTX</b>	<b>+</b>	+	-	R-CTx + Surgery	CR		DOC
74	M	Rectum	<b>Infliximab</b>	<b>+</b>	-	-	R-CTx	CR	52	DD
47	F	Duodenum	<b>Tacrolimus</b>	<b>+</b>	-	-	R-CTx	PR		AWD
57	M	Jejunum	<b>Synchronous GC</b>	<b>+</b>	-	-	R-CTx + Surgery	CR		NED
66	M	Ileocecum	Old age	<b>+</b>	-	-	R-CTx + Surgery	CR		NED
71	M	Jejunum	RC	-	+	-	R-CTx + Surgery	PR		DOC

# Neoplastic PD-L1+ Extranodal DLBCLs

- 全臨床経過を通して、節外臓器浸潤により特徴付けられる
- 血管“内”あるいは“外”増殖を超えた臨床病理学的特徴に着目される
- 少なくとも免疫逃避に依拠する節外性DLBCLとしての包括化は可能
- 用語は、単純にコンセンサスの問題
- **SP142で認識されるPD-L1発現が最も機能的！**
- 中枢神経・睾丸原発DLBCLにおけるPD-L1、さらなる検証が必要

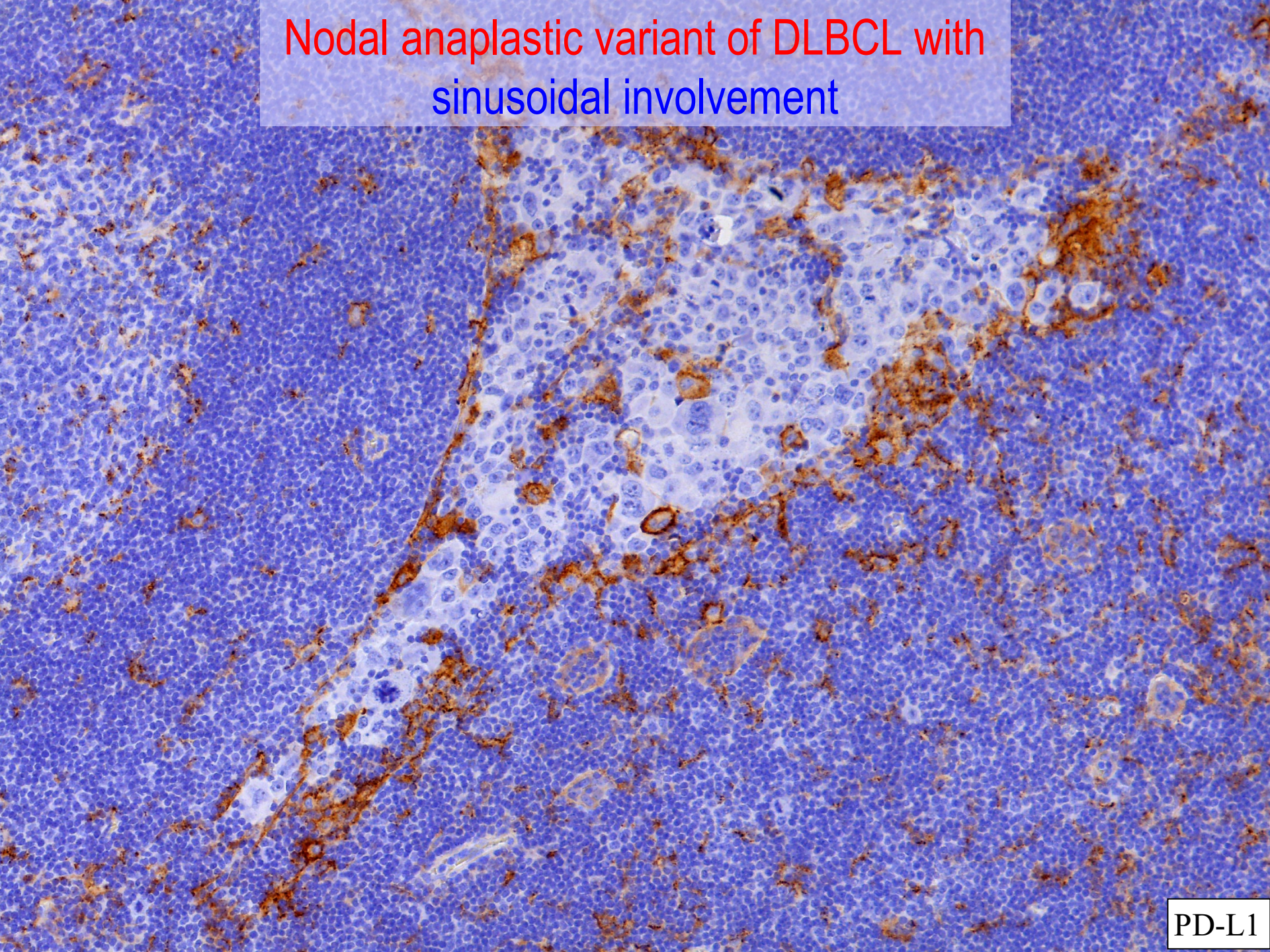


# Peripheral deletion mediated by PD-L1 expression on lymphatic endothelial cells (LECs) in lymph nodes (*Blood* 2012;120:4664).





Nodal anaplastic variant of DLBCL with  
sinusoidal involvement



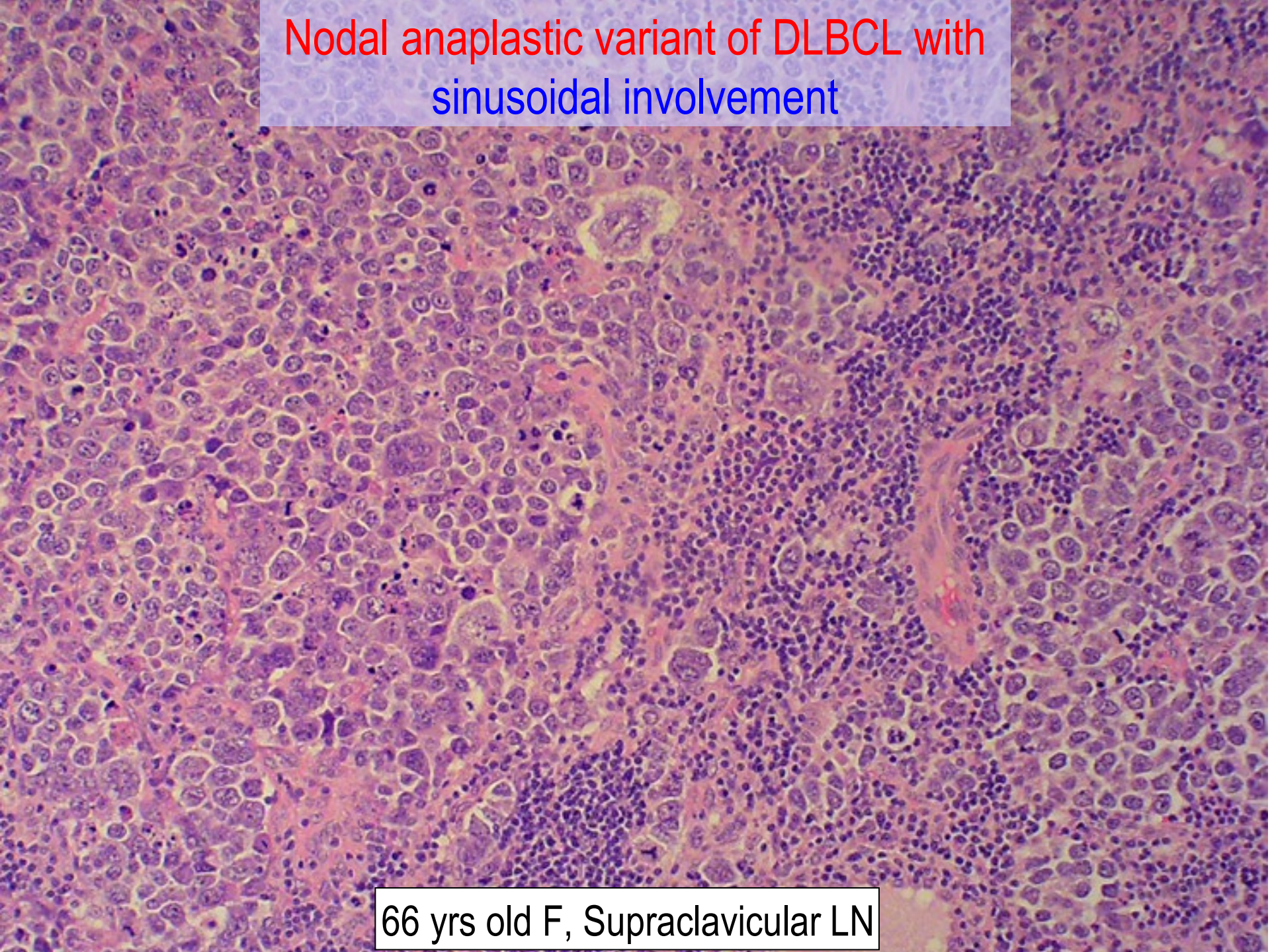


# Anaplastic variant of DLBCL: Reappraisal as a Nodal Disease with Sinusoidal Involvement (Megahed NA et al. *Pathol Int* 2019)

- Lai R, Medeiros LJ, Dabbagh L, Formenti KS, Coupland RW. **Sinusoidal CD30-Positive Large B-cell Lymphoma**: A Morphologic Mimic of Anaplastic Large Cell Lymphoma. *Mod Pathol* 2000;13:223
- 11 cases, 5 male and 6 female, with a median of 63 yrs (range, 36 to 82), 8 patients (73%) elder than 60 yrs old
- CD3-, CD20+ (in 9 of 11, 82%), CD30+, ALK-, EBV-
- Nodal disease with a sinusoidal growth pattern in all and foci of confluent tumor cell growth in 4 of 11
- All contained large pleomorphic and/or HRS-like cells
- 6 of 10 pts died of disease with a median survival of 13 months.

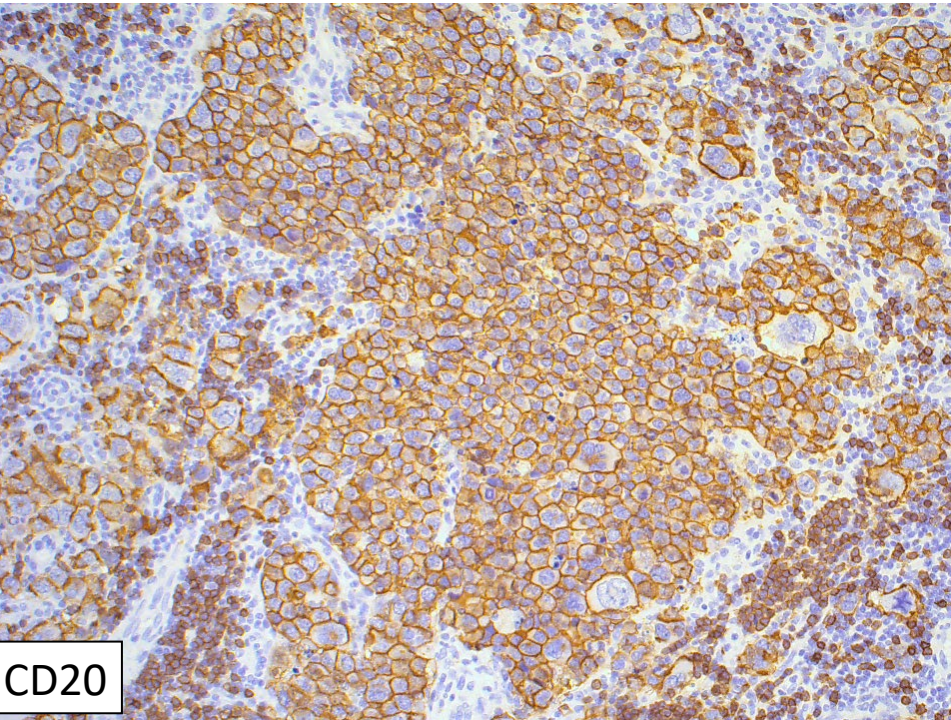


Nodal anaplastic variant of DLBCL with sinusoidal involvement

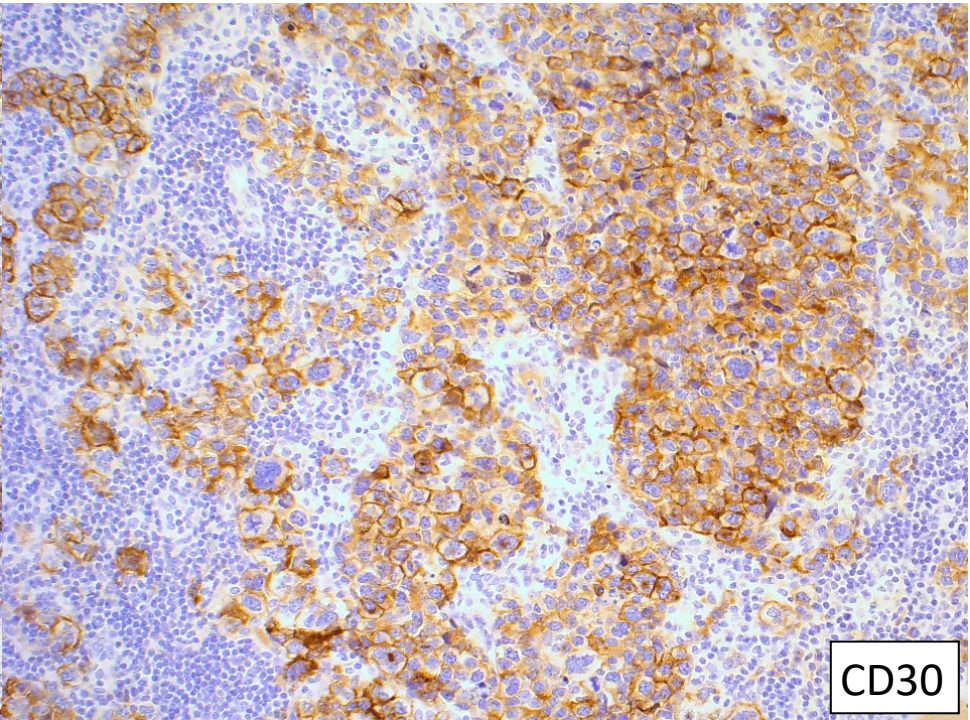


66 yrs old F, Supraclavicular LN

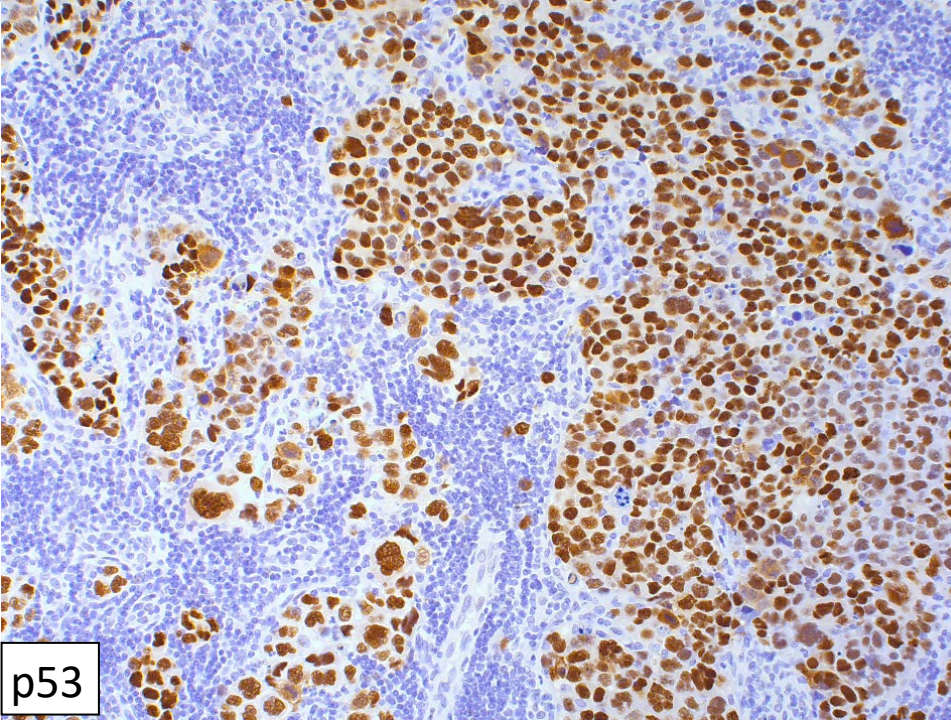




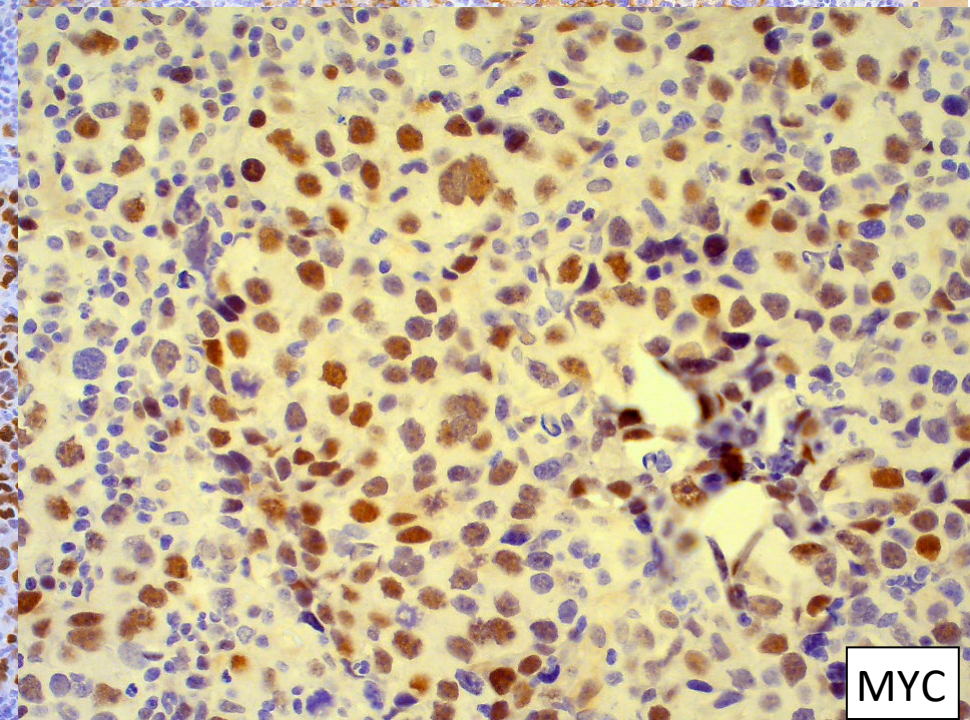
CD20



CD30

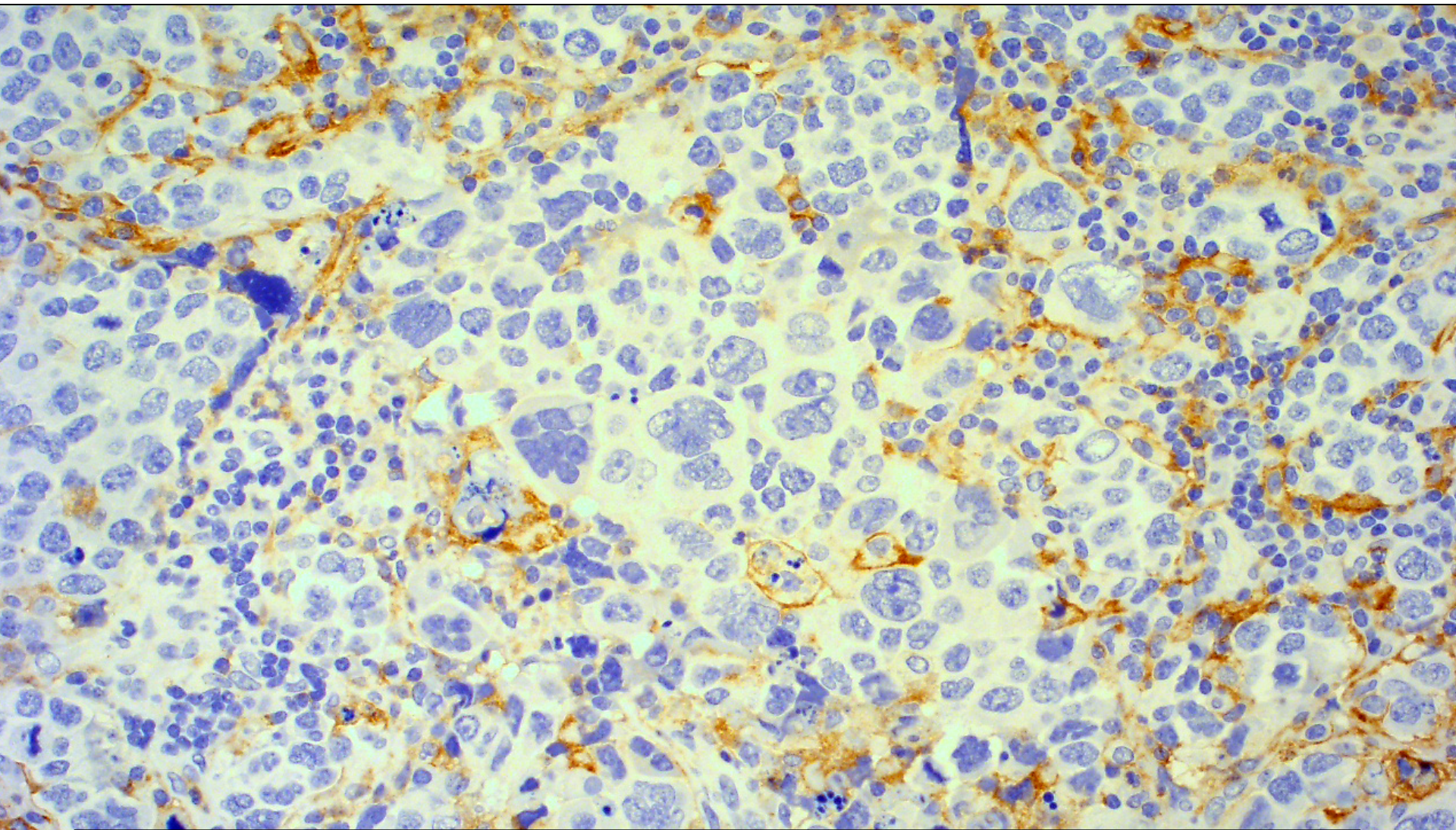


p53



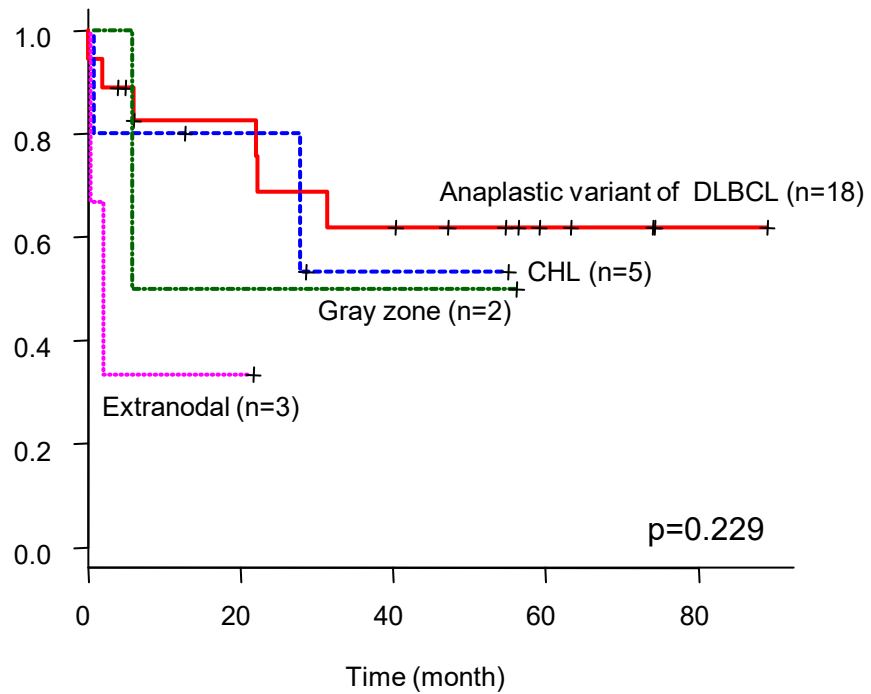
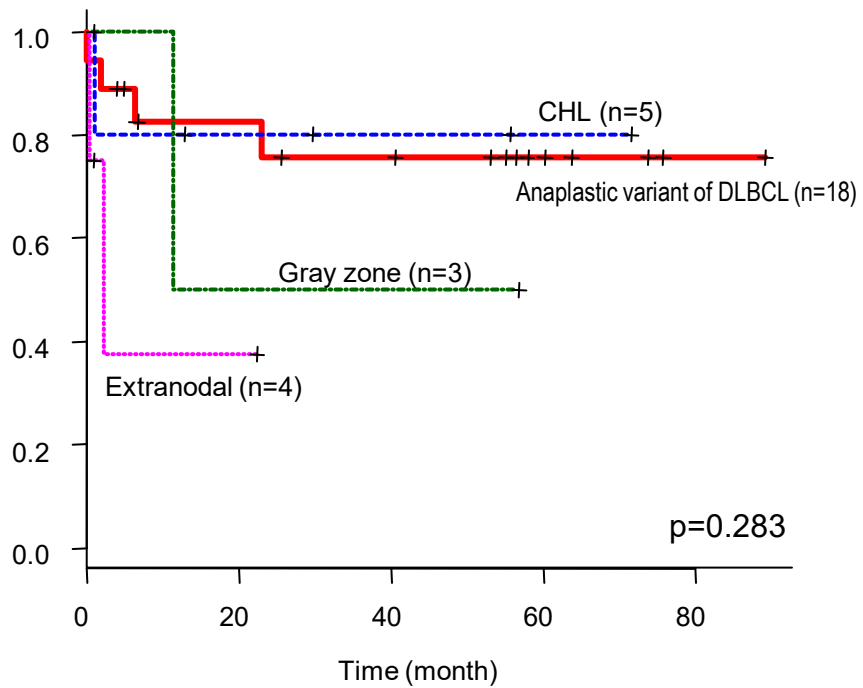
MYC



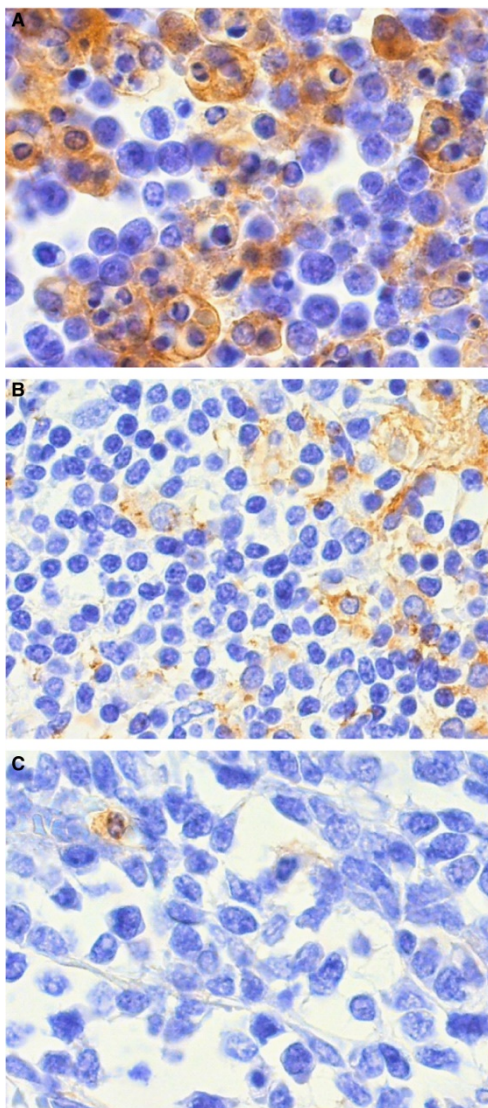


PD-L1 immunostain shows an image of a framing pattern with a compartmentalization of the tumor cells by being surrounded by PD-L1-positive non-tumor cells

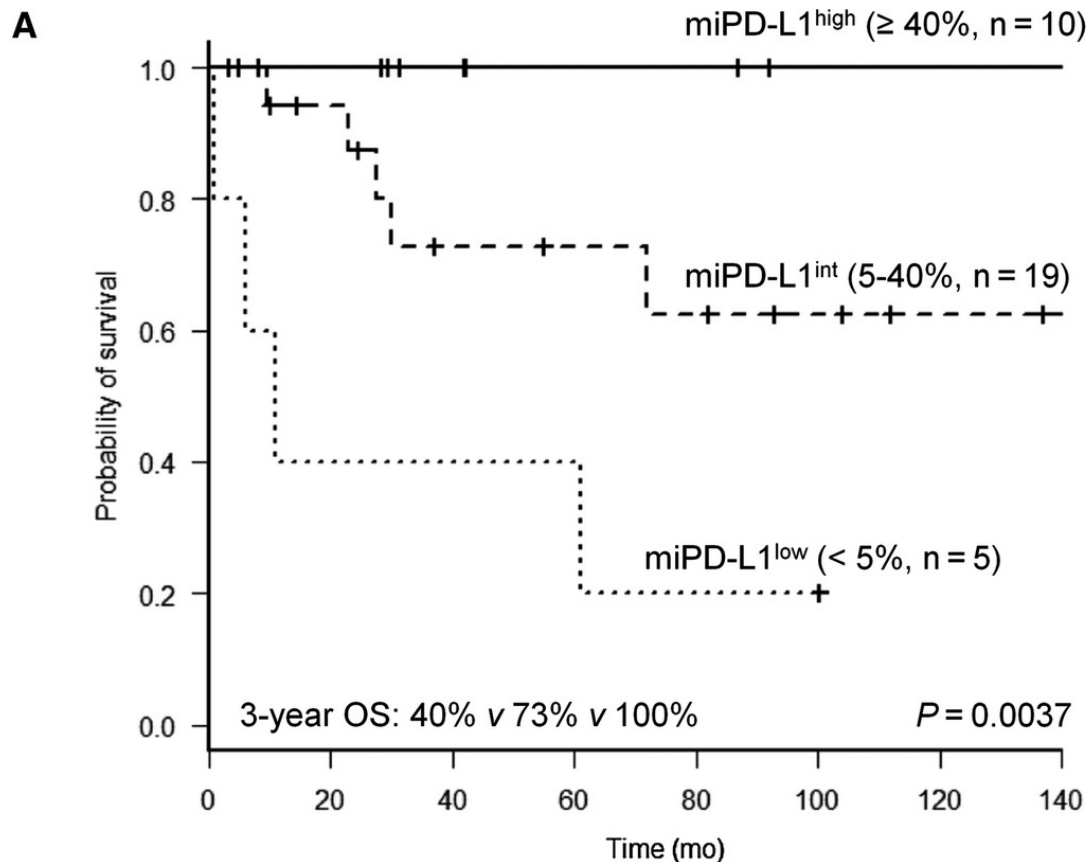




# Clinicopathological analysis of primary intestinal DLBCL: Prognostic evaluation of CD5, PD-L1, and EBV on tumor cells



PD-L1



miPD-L1	Number at risk	0	20	40	60	80	100	120	140
high (≥ 40%)	10	8	5	3	3	1	1	1	1
int (5-40%)	19	14	8	7	6	4	2	1	1
low (< 5%)	5	2	2	2	1	1	0	0	0



# PD-L1発現の臨床病理学的意義： B細胞リンパ腫

## 節外性びまん性大細胞型B細胞リンパ腫 特殊型

- 1) 血管内大細胞型B細胞リンパ腫
- 2) 系統的な節外浸潤により特徴付けられる、  
経過を通じて節性病変はまれ
- 3) 形態（組織像）と免疫逃避、いずれが定義  
に重要か？

# リンパ腫研究：臨床病理学的解析

- 1) 血管免疫芽球型T細胞リンパ腫
- 2) 未分化大細胞型T細胞リンパ腫
- 3) MALTリンパ腫
- 4) マントル細胞リンパ腫
- 5) 加齢性EBV関連B細胞リンパ増殖異常症  
EBV陽性DLBCL
- 6) 節性細胞傷害性分子陽性T細胞リンパ腫
- 7) 血管内大細胞型リンパ腫
- 8) . . . など、など





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PUBLICATIONS IN  
WEB OF SCIENCE

628

SUM OF TIMES  
CITED

19,673 74<sup>②</sup>

H-INDEX

AVERAGE  
CITATIONS PER  
ITEM

31.4

AVERAGE  
CITATIONS PER  
YEAR

531.7

## Peer review metrics

VERIFIED REVIEWS

0

Median: 3  
3th percentile

VERIFIED REVIEWS (LAST 12 MONTHS)

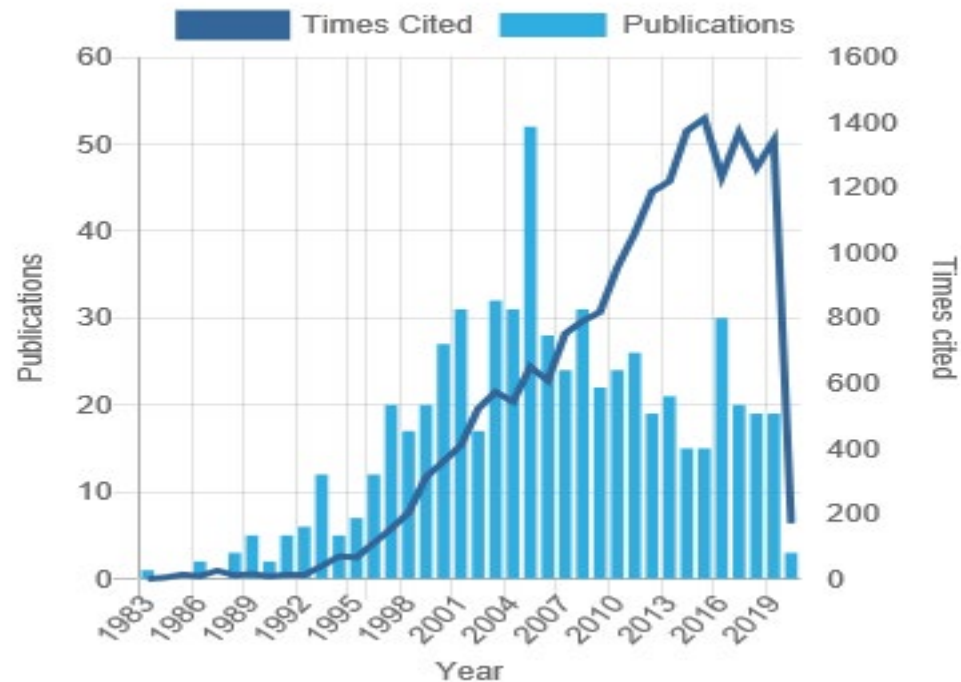
0

Median: 1  
34th percentile

REVIEW TO PUBLICATION RATIO

-

Median: 0.3:1





Shigeo Nakamura

ResearcherID

14/Nov/2019

H index 73

Citation 19224



Elaine Jaffe

Google Scholar

14/Nov/2019

H index 181

Citation 160983







STAFF  
名古屋大学

第58回 リンパ網内系学会総会  
2018年6月28日-30日  
名古屋大学  
宇利 兼秀

第58回 リンパ網内系学会総会  
2018年6月28日-30日

- Age-related **EBV**-associated B-cell lymphoproliferative disorders and other **EBV+** lymphoproliferative diseases: new insights into immune escape and senescence or immunodeficiency through staining with anti-PD-L1 antibody clone SP142
- Running title: PD-L1 immunostaining of EBV+ B-LPDs
- Ayako Sakakibara, MD,<sup>1</sup> Kei Kohno, MD,<sup>1</sup> Eri Ishikawa, MD,<sup>1</sup> Yuka Suzuki, MD,<sup>1</sup> Satoko Shimada MD,<sup>1</sup> Ahmed E. Eladl MD,<sup>2</sup> Ahmed A. Elsaved MD,<sup>2</sup>

> Reviewer: 2

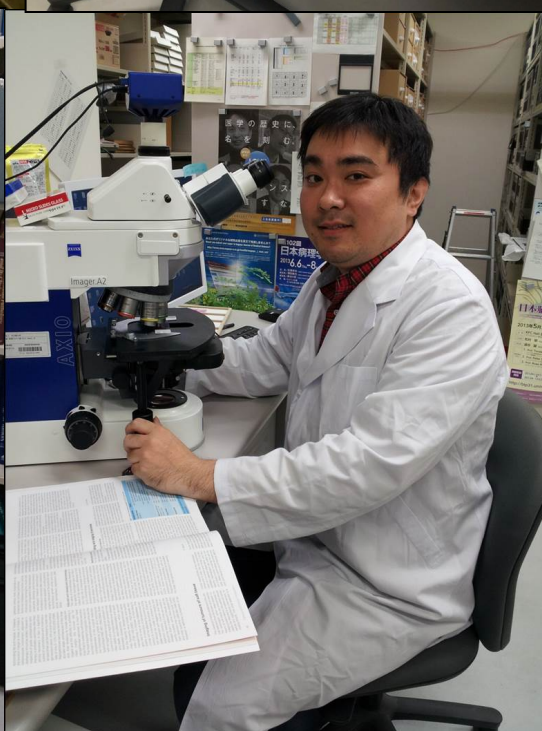
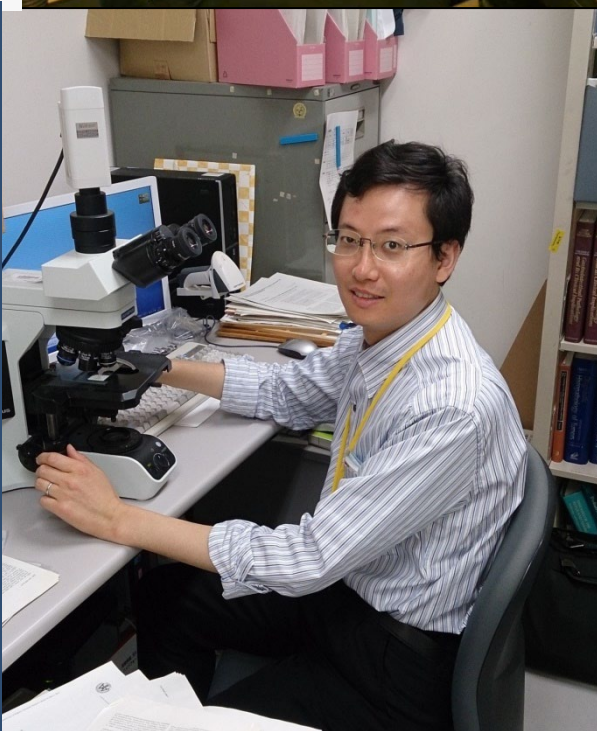
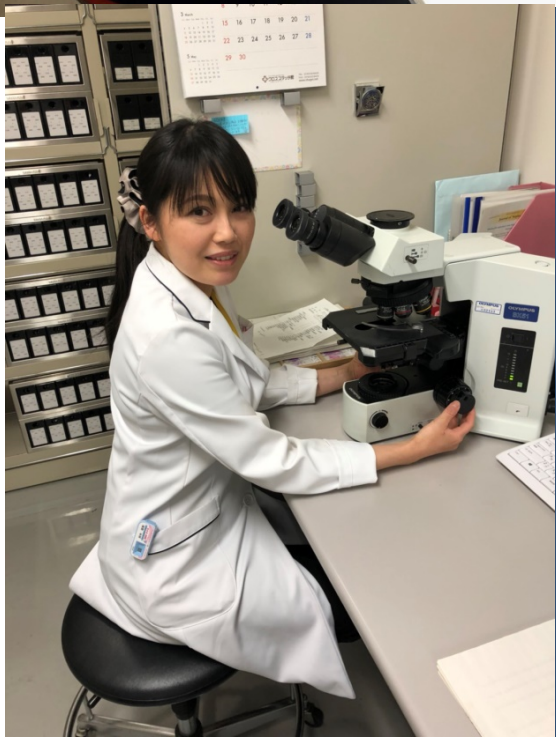
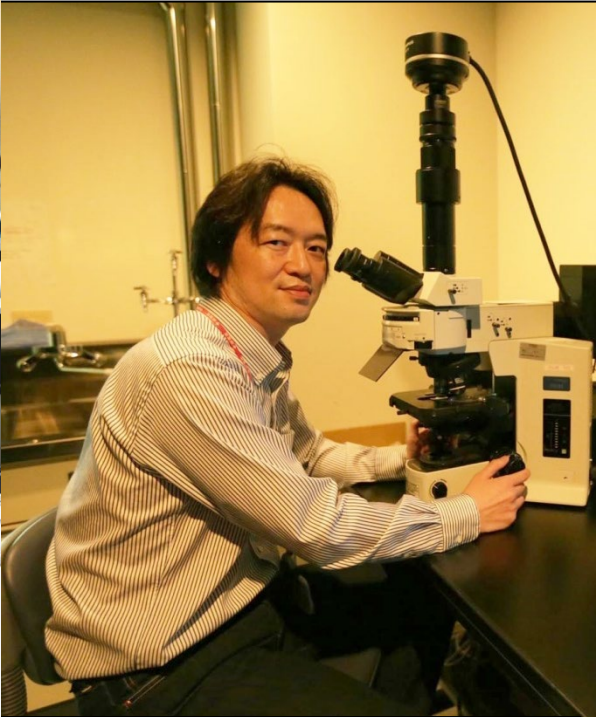
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> Comments to the Author

> リンパ増殖性疾患と免疫不全、EBV、PD-L1について考察されている独創的なreviewだと思います。



1. The authors propose that there is a difference between immune escape based on neoplastic expression of PD-L1 on tumor cells, and Immune senescence without expression of PD-L1 on tumor cells, and **a combined group**, in which both factors may be involved. Unfortunately, they provide almost **no data** to address this hypothesis. The hypothesis is just based on staining reported, and not on known mechanisms that cause upregulation of PD-L1/12 on tumor cells via gene amplification or rearrangement. **Such data do exist** from other groups that have studied this point, but those data are not referenced.





## Is this too complicated?

“The immune system is complex... (therefore) the tumors derived from it will be numerous.”

Karl Lennert

“Everything should be made as simple as possible, but not simpler.”

Albert Einstein





# Interdigitating Dendritic Cell Sarcoma (*Nakamura S et al. Cancer 1988;61:2562*)

- 指状嵌入樹状細胞肉腫、極めてまれな腫瘍
- 58歳男性、1982年、左頸部リンパ節の腫脹を主訴に来院、生検診断は悪性リンパ腫、分類不能型、ただしホジキンリンパ腫との鑑別が問題となる。CHOPにて治療するも、1986年、空腸に二度にわたり再発、外科的切除、腸間膜リンパ節に浸潤を伴う。
- 1990年、肺炎にて死亡、診断より101ヵ月。
- 遺言により剖検を施行、腫瘍残存なし

# リンパ腫分類：今、何が問題か？

- ・ ホジキン型腫瘍の再定義

免疫臓器（リンパ節、胸腺、**小腸？**）に発生する免疫逃避を基盤とする免疫細胞由来の腫瘍である



