

20 novembre 2020

Journée annuelle des histiocytoses

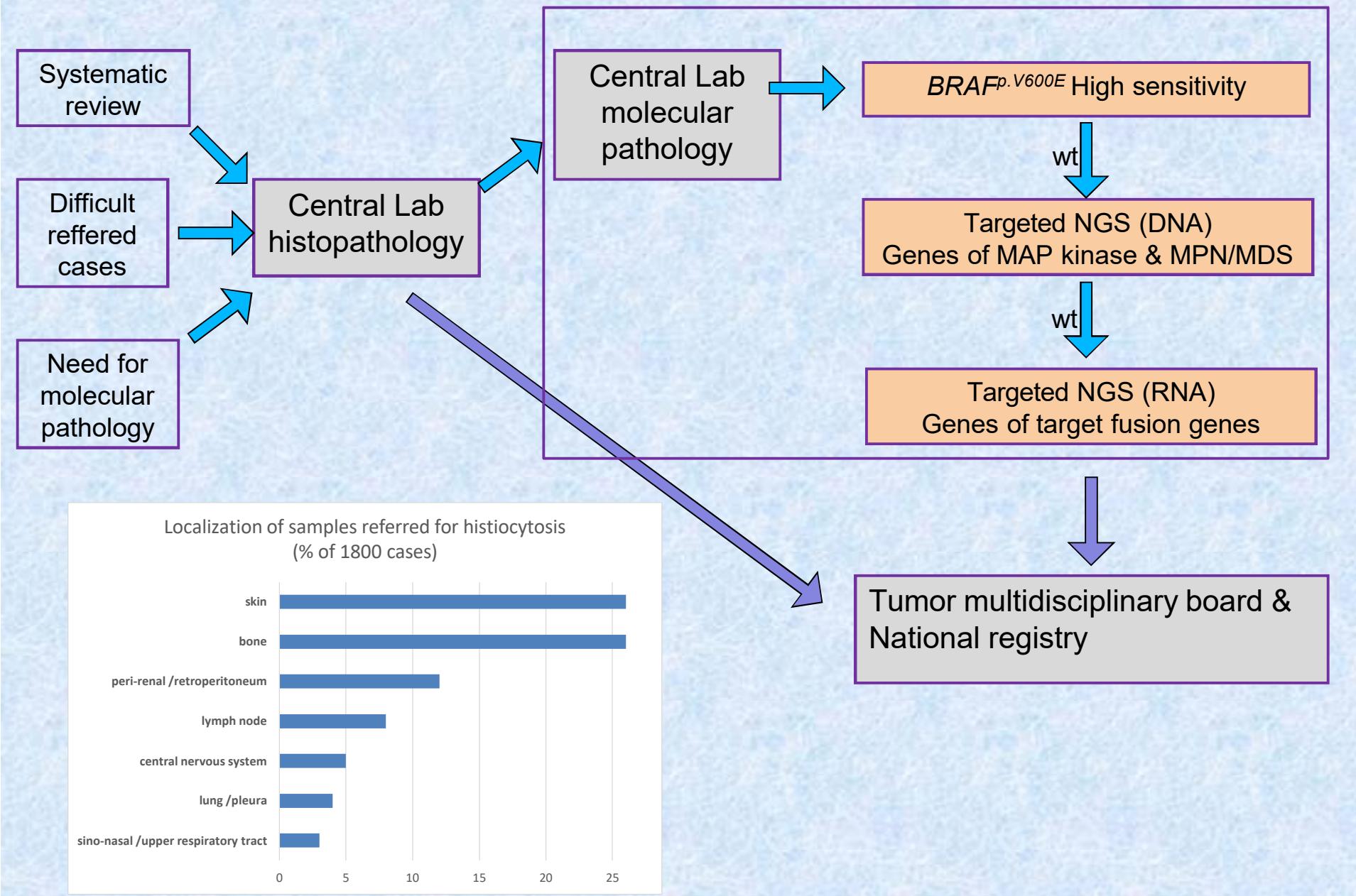
Actualités histopathologie et pathologie moléculaire

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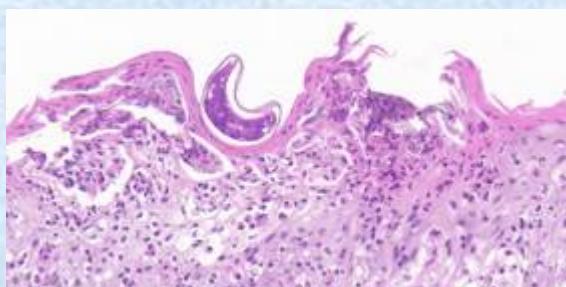
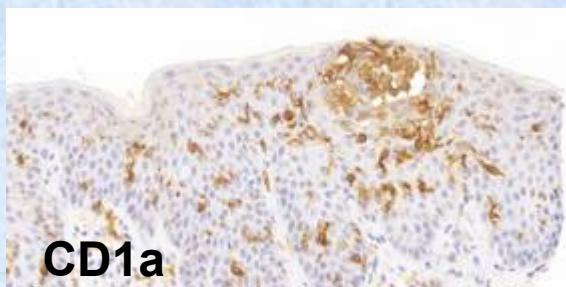
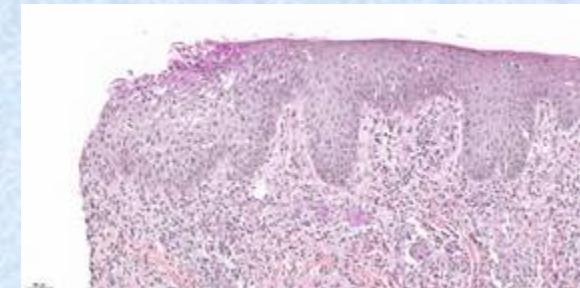
Jean-francois.emile@uvsq.fr

Systematic histological & molecular review in France

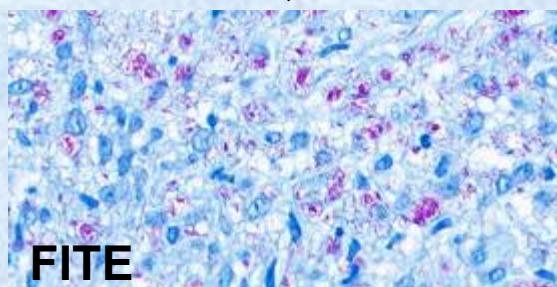
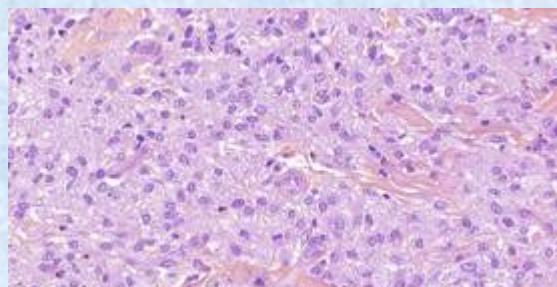
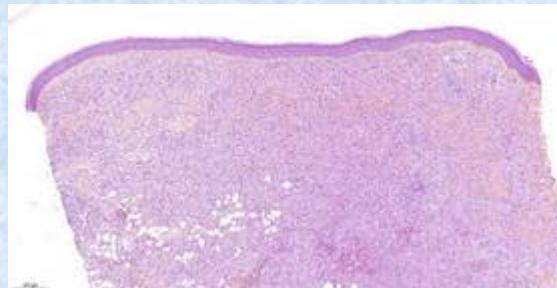


Intérêt d'une relecture systématique ?

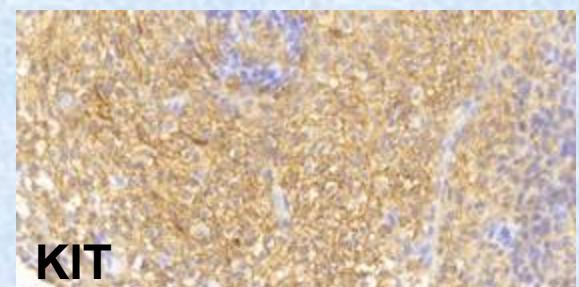
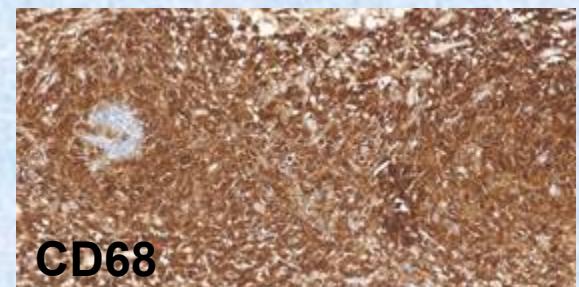
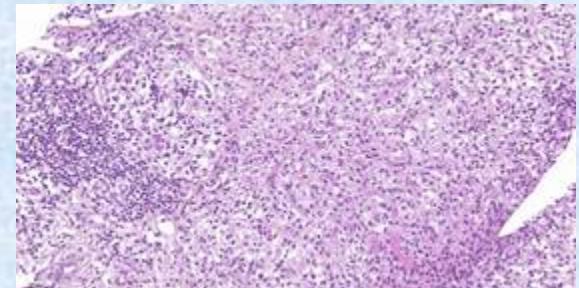
3 months old baby
Disseminated skin lesions



23 years old female
Several skin papules

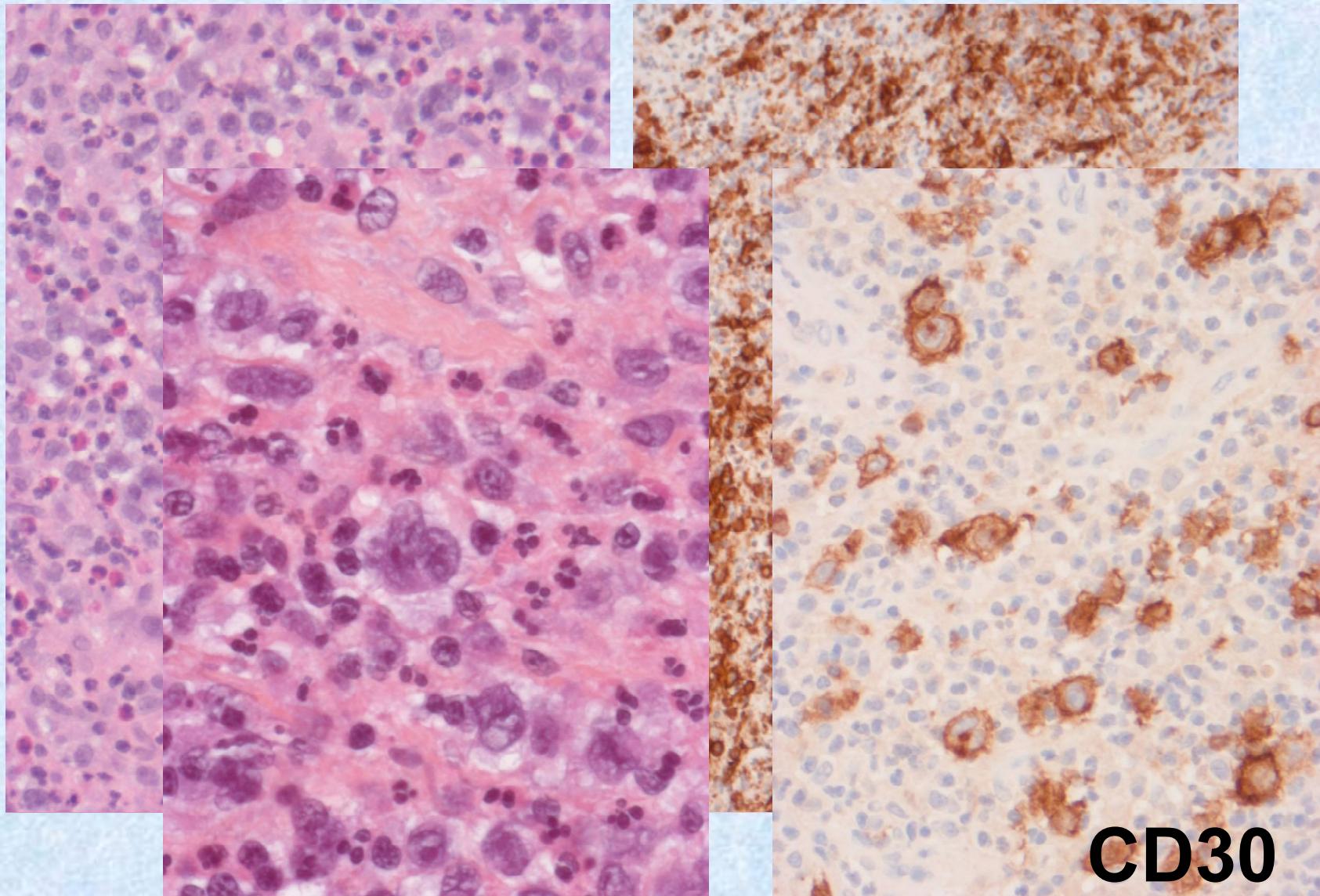


60 years old female
Polyadenopathies
hepatosplenomegaly



Mastocytosis

Intérêt d'une relecture systématique ?



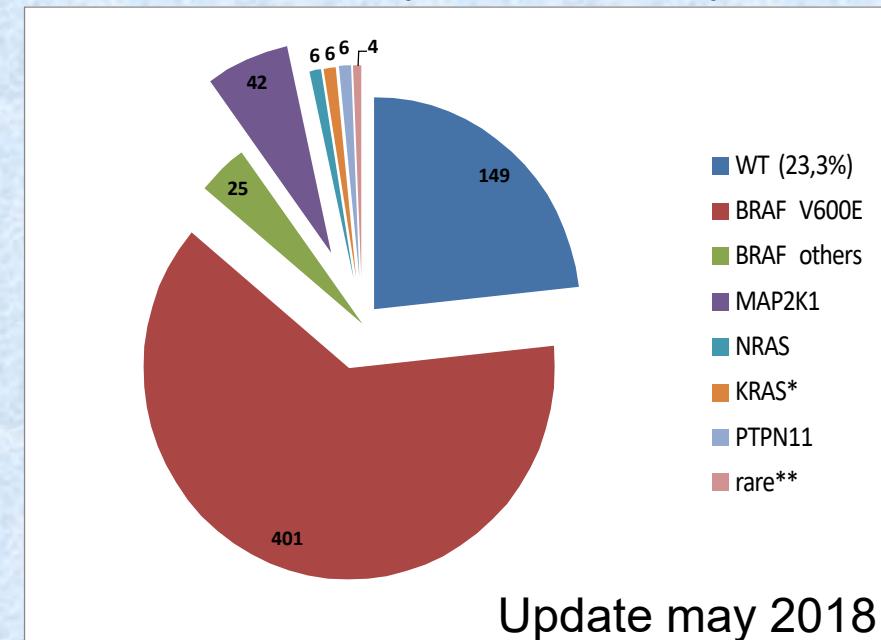
JF 15 ans. Lésion costale lytique
Maladie de Hodgkin classique

CD30

Analyses mutationnelles

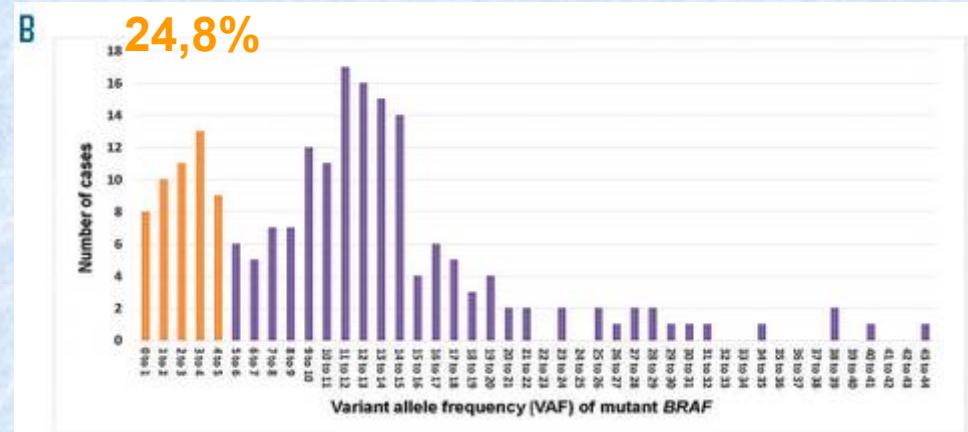
Frequency of the mutations

639 samples all types of histiocytoses



Mutation detection should be performed:

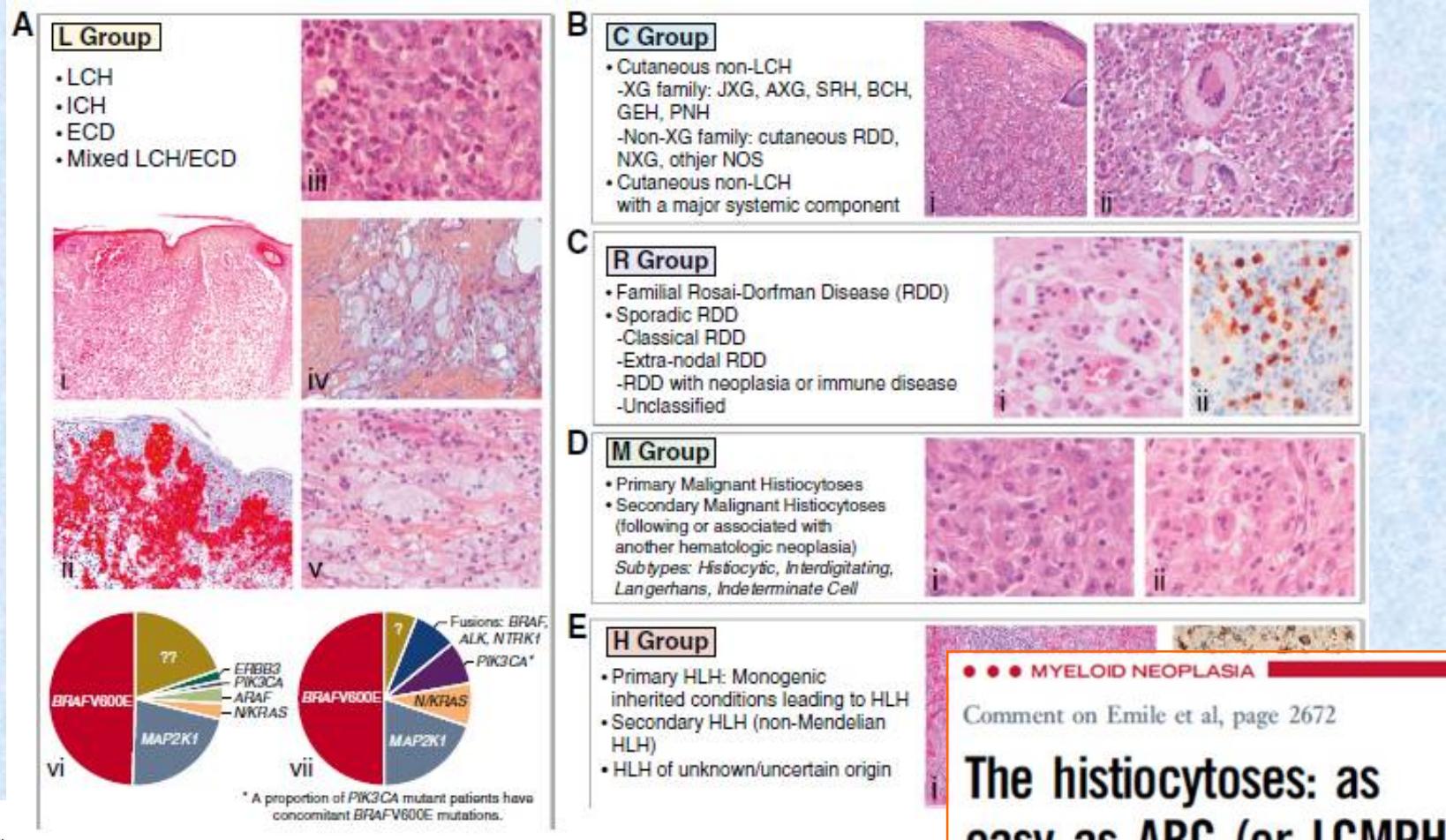
- . in experienced lab(>30 cases /year)
- . using methods with high sensitivity



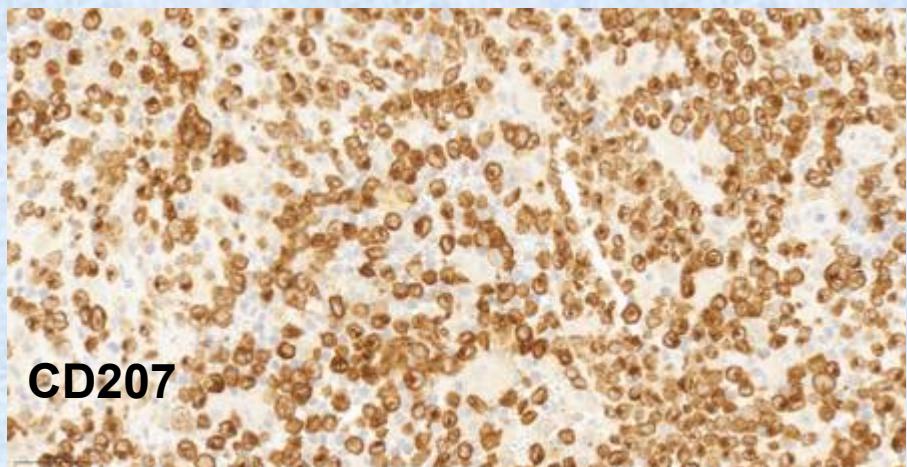
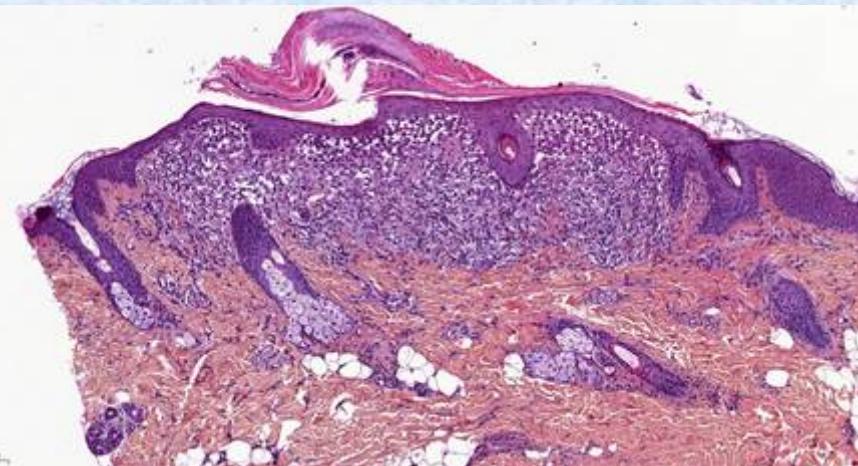
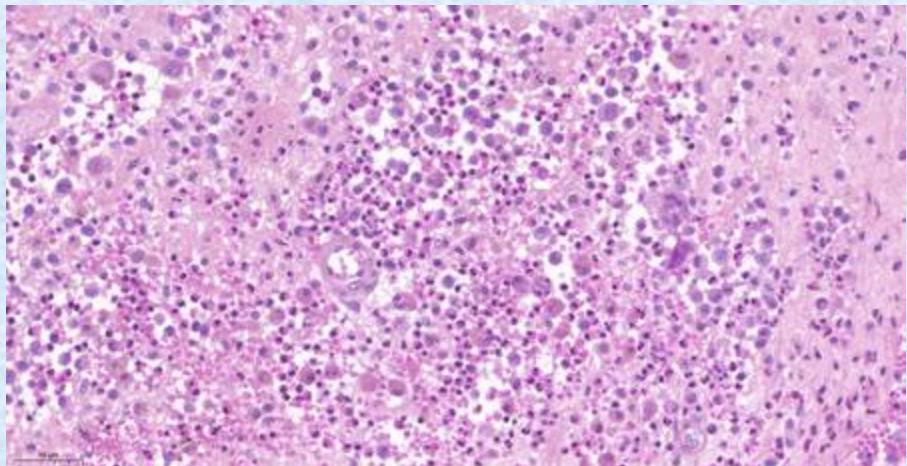
Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages

Jean-François Emile,^{1,2} Oussama Abla,³ Sylvie Fraitag,⁴ Annacarin Horne,⁵ Julien Haroche,^{6,7} Jean Donadieu,^{1,8} Luis Requena-Caballero,⁹ Michael B. Jordan,¹⁰ Omar Abdel-Wahab,¹¹ Carl E. Allen,¹² Frédéric Charlotte,^{7,13} Eli L. Diamond,¹⁴ R. Maarten Egeler,³ Alain Fischer,^{15,16} Juana Gil Herrera,¹⁷ Jan-Inge Henter,¹⁸ Filip Janku,¹⁹ Miriam Merad,²⁰ Jennifer Picarsic,²¹ Carlos Rodriguez-Galindo,²² Barret J. Rollins,^{23,24} Abdellatif Tazi,²⁵ Robert Vassallo,²⁶ and Lawrence M. Weiss,²⁷ for the Histiocyte Society

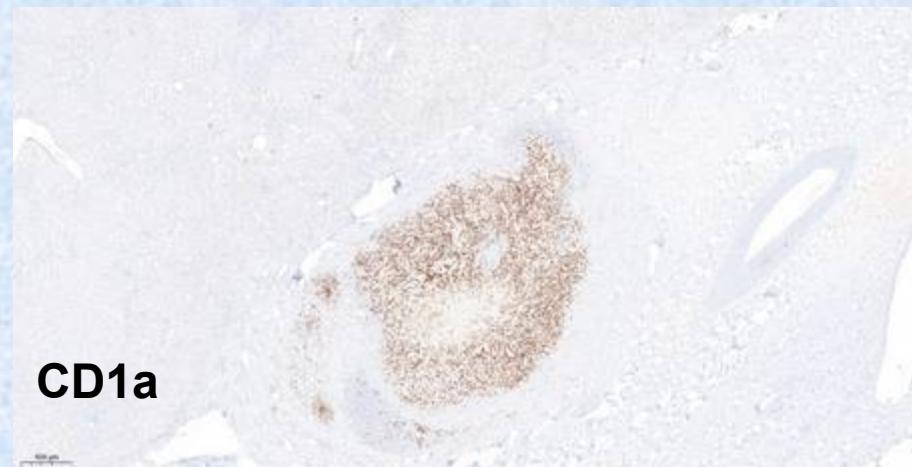
BLOOD, 2 JUNE 2016 • VOLUME 127



Langerhans cell histiocytosis (LCH)



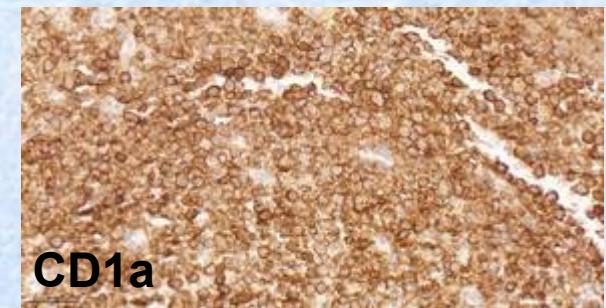
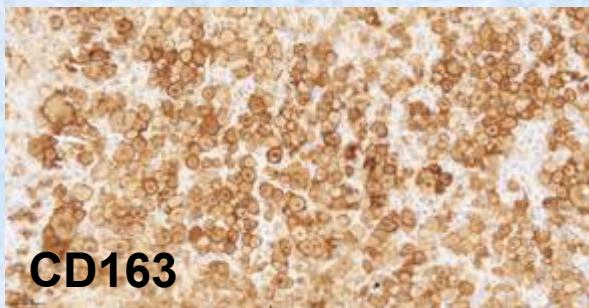
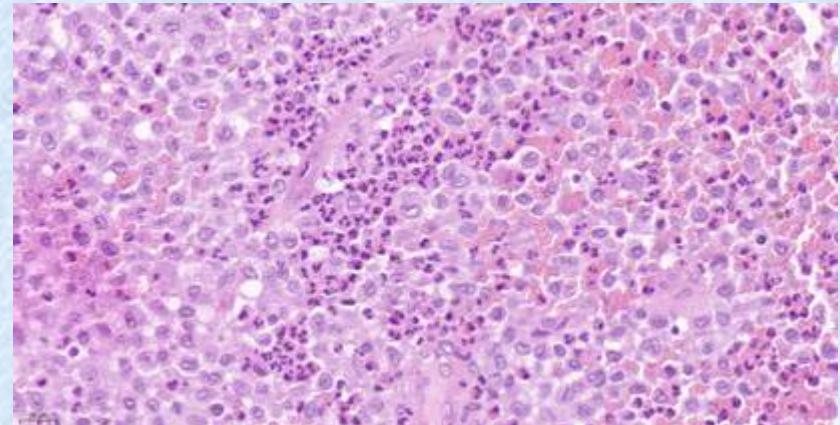
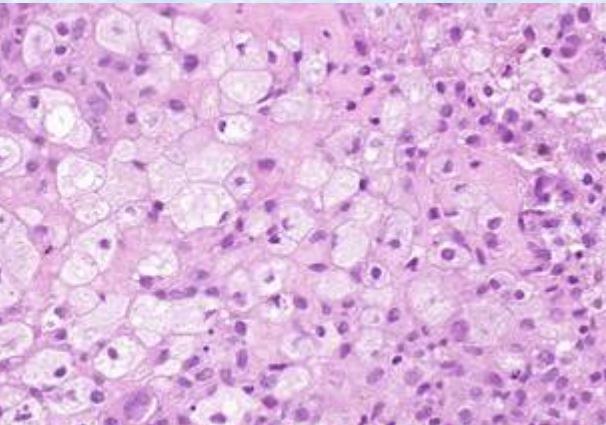
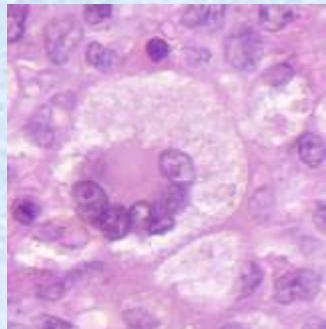
CD207



CD1a

Use both CD1a and CD207
Spare the sample for molecular analysis

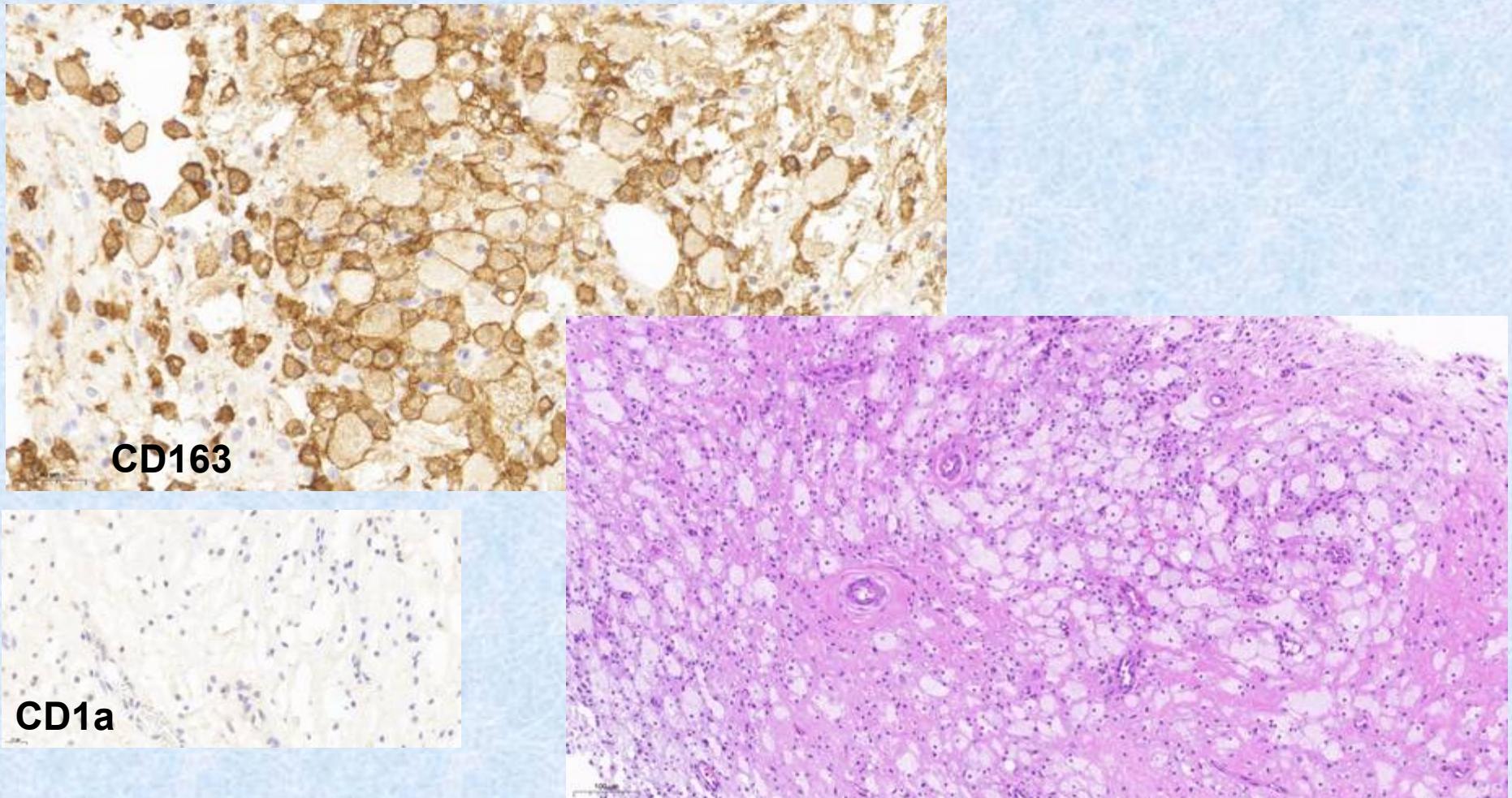
Histiocytoses du groupe L : formes de passage



4 years old boy with one lesion of the skull, probably since >6months

- « old LCH » with xanthomization of histiocytes?
- Mixed type (Erdheim Chester & LCH) histiocytosis?

Histiocytoses du groupe L : formes de passage



14 year old boy with unique intra-cerebral tumor. *BRAF* V600E mutation

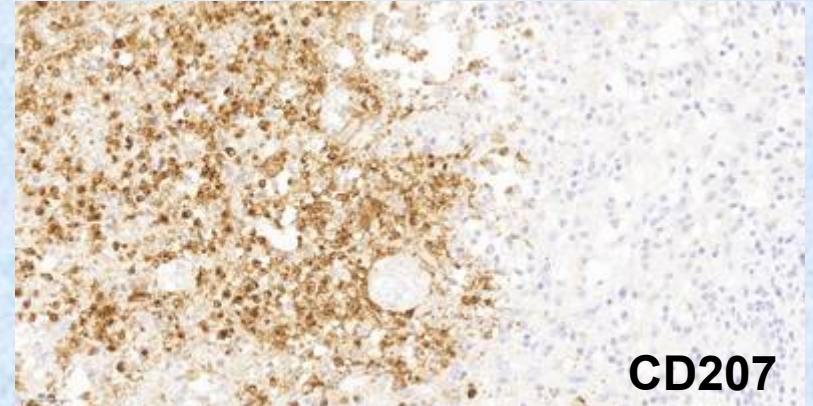
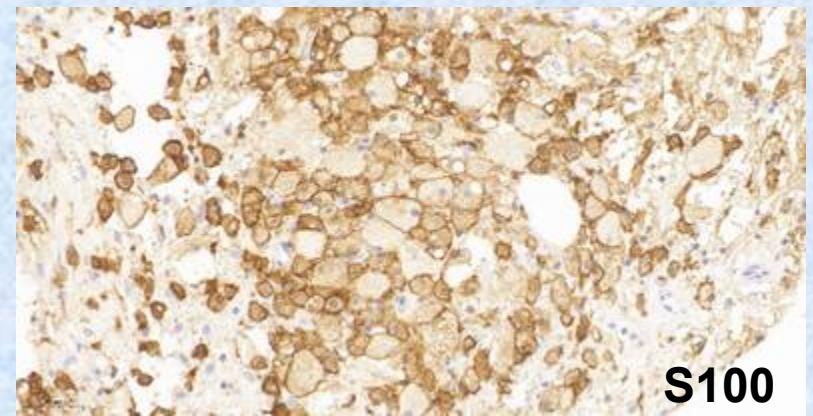
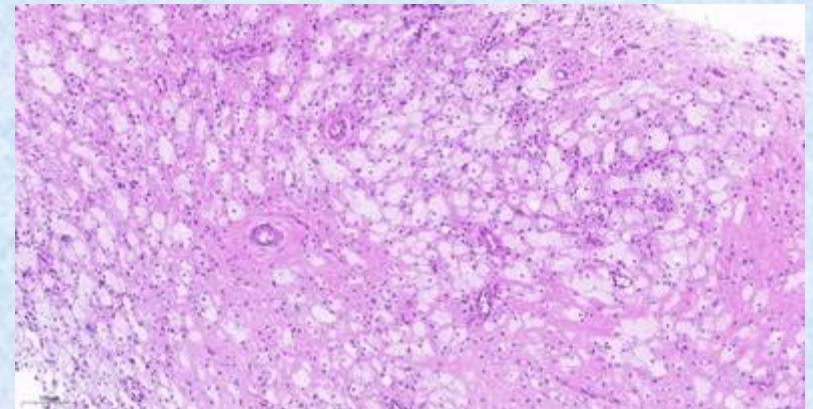
- Extra-cutaneous Xanthogranuloma?
- L group histiocytosis?

Histiocytoses du groupe L : formes de passage



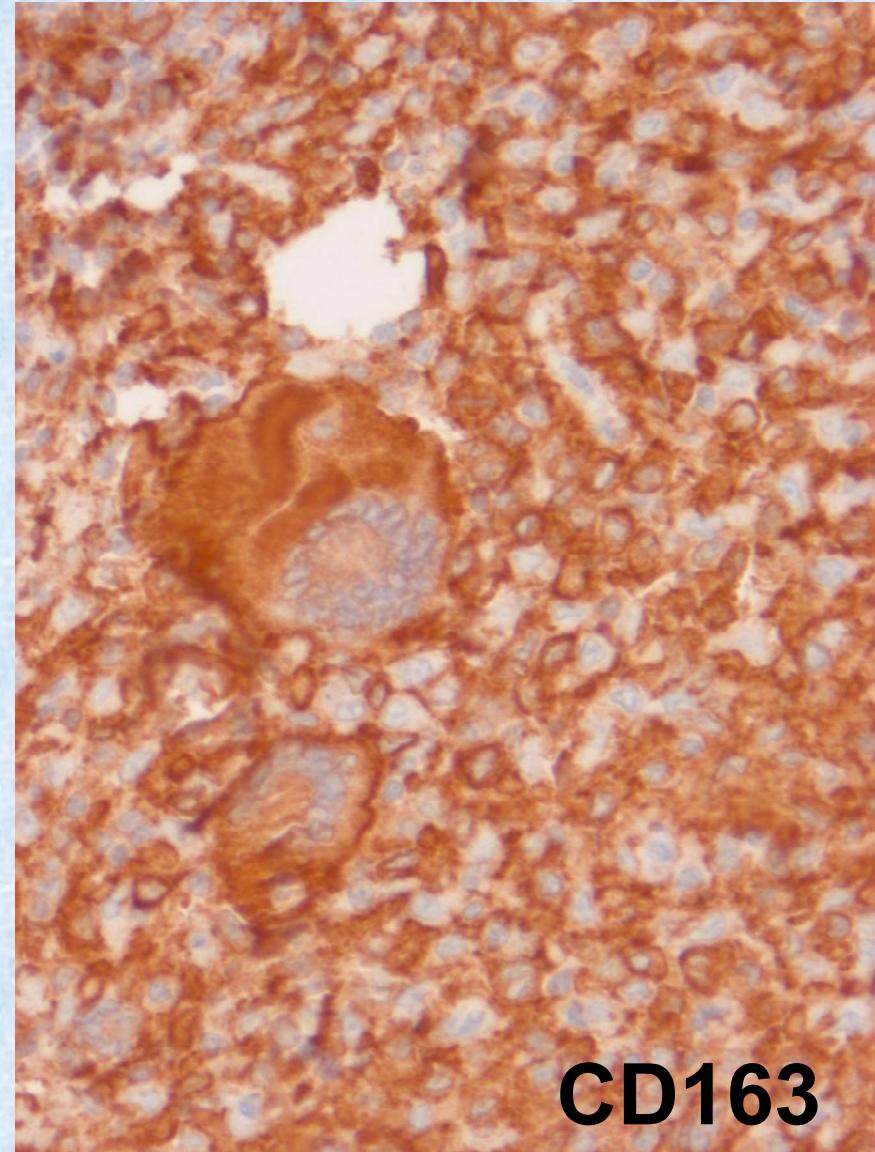
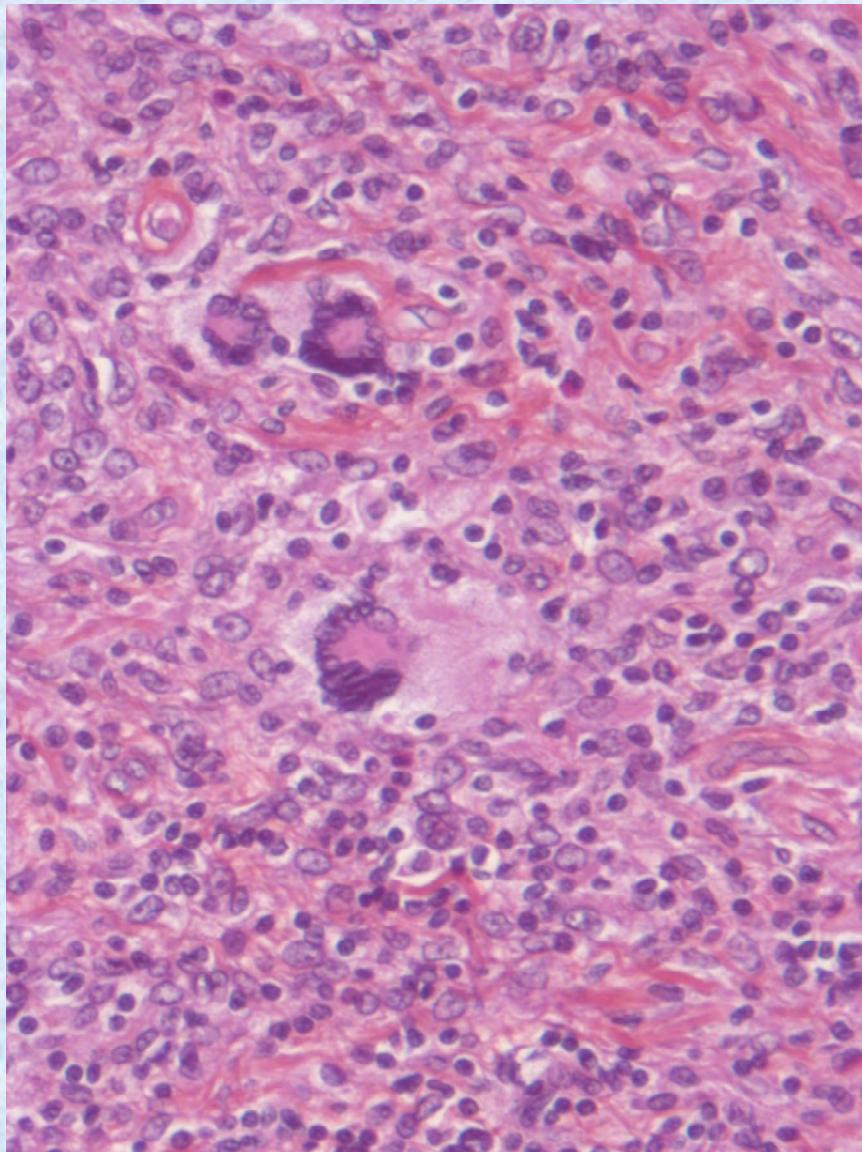
Muma et al. Lancet 2019

4 years old child
widespread lymphadenomegaly &
one lytic lesion of the skull

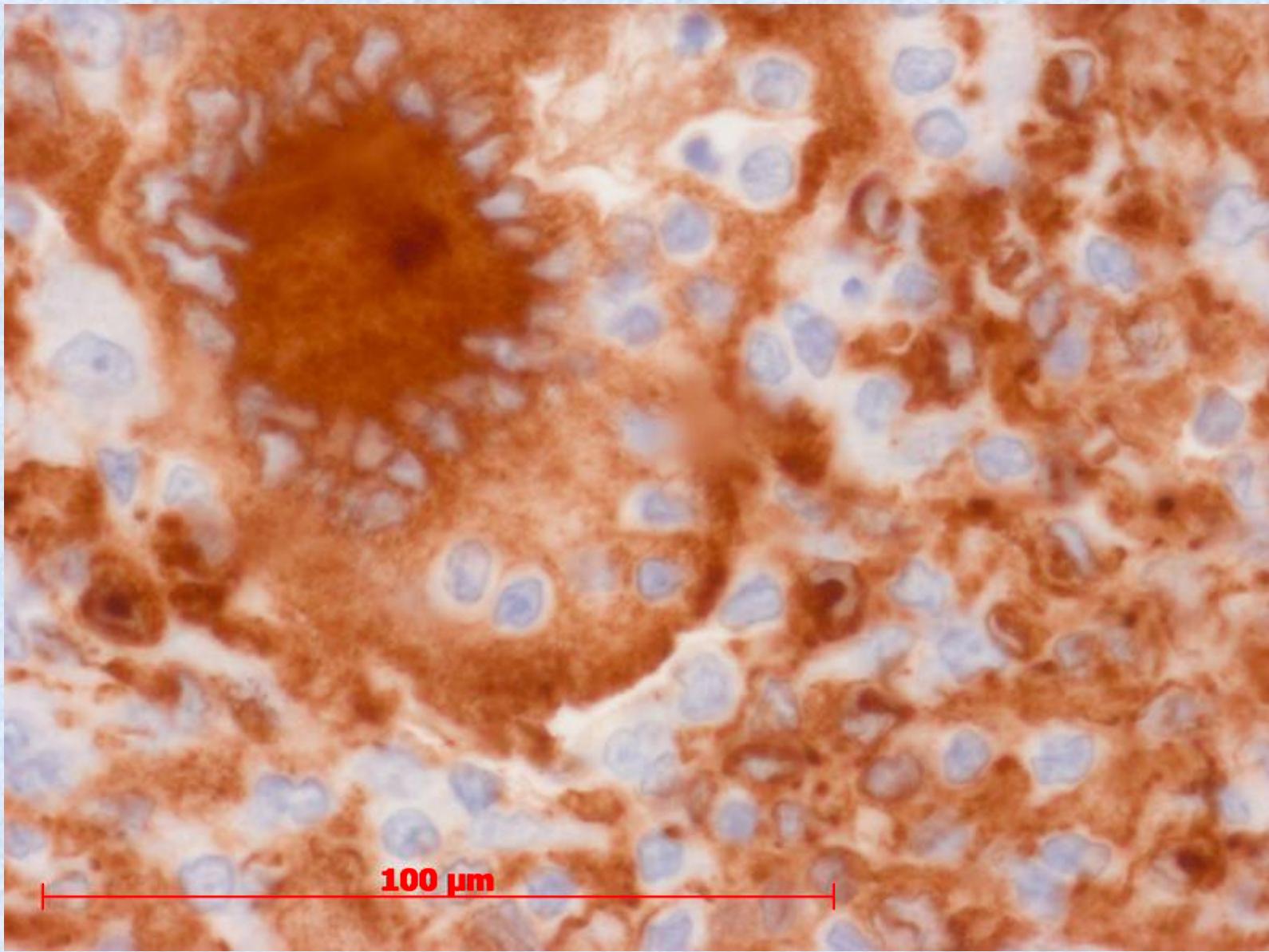


- Mixed type (Rosai-Dorfman & LCH) histiocytosis with *MAP2K1* mutation

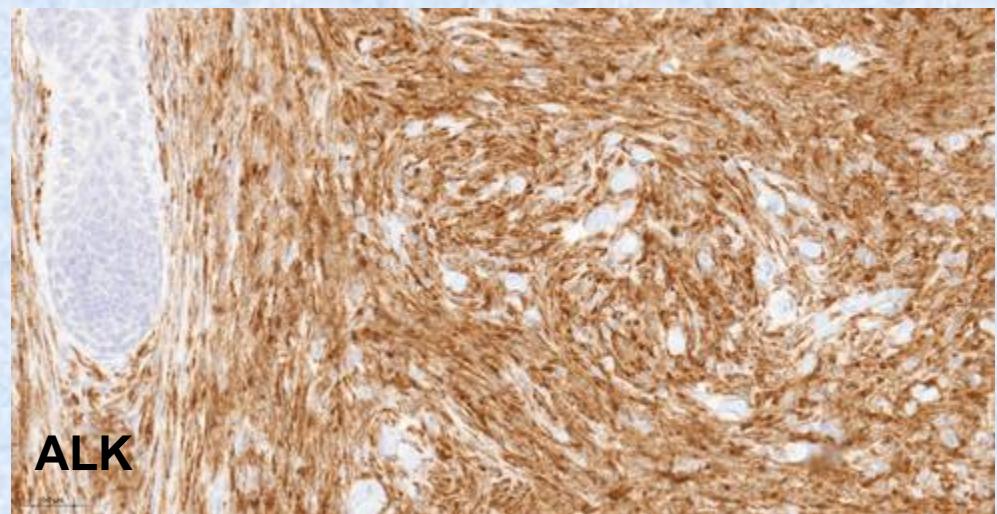
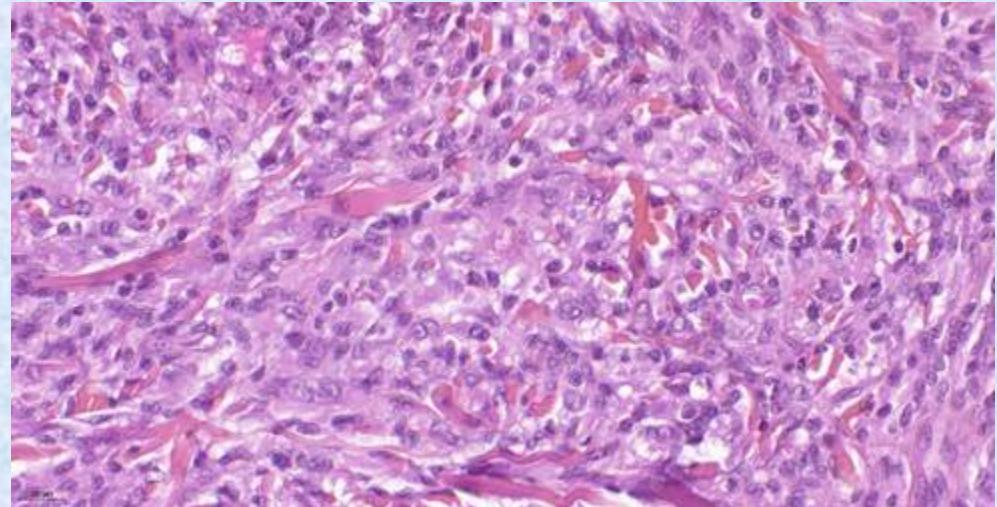
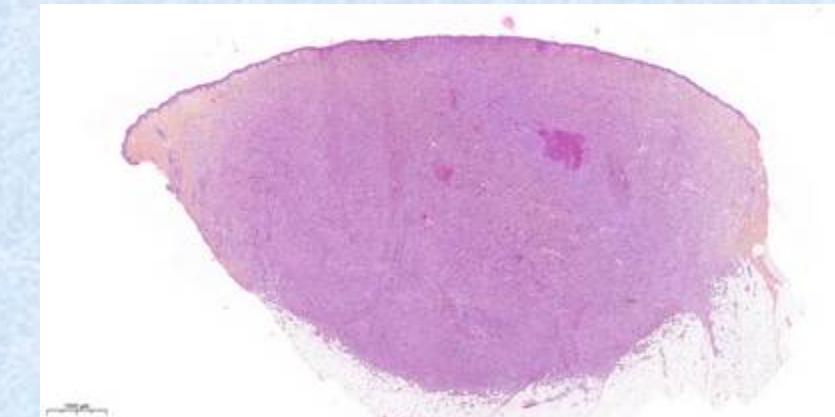
Histiocytoses du groupe L : Histiocytose ALK+



Histiocytose ALK+



Emerging entities in L group



2 years old female with single cervical nodule. *ALK* fusion

- ALK+ histiocytosis

Emerging entities in L groups

ALK+ histiocytosis:

Probably some cases were reported as JXG

Very heterogeneous presentation; among pediatric referred cases:

- 2 years old girl with single small skin nodule
- 6 month girl with liver, bone, lung & CNS involvement
- 13 years old male with single large CNS tumour

Response to treatment:

- Some with excellent response to targeted therapy (alectinib)
- Some with excellent response to VLB-prednisone

Indeterminate cell histiocytosis:

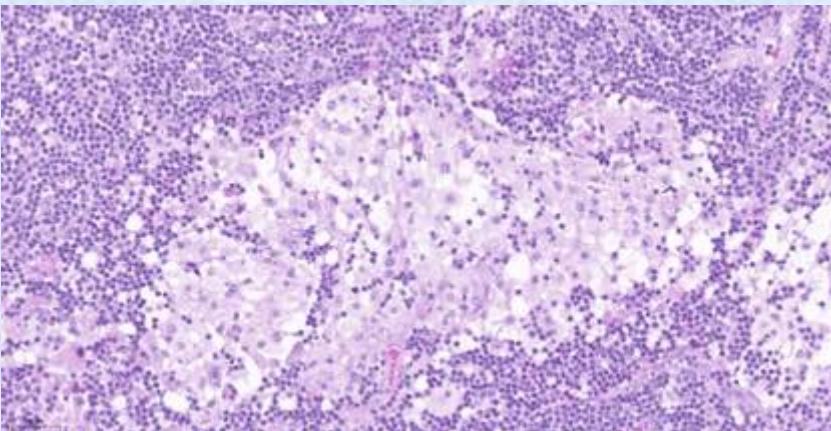
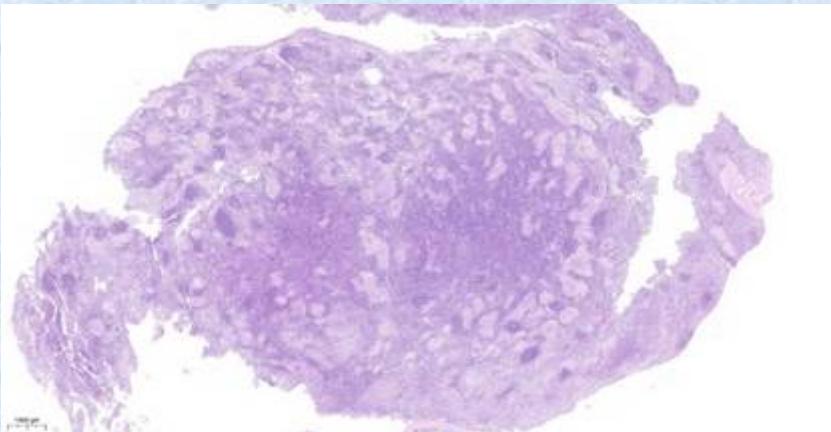
Similar to LCH, but CD207 negative

Some cases with *ETV6-NCOA2* fusion gene,
but not specific and some patients have *BRAF* V600E

Among our referred cases:

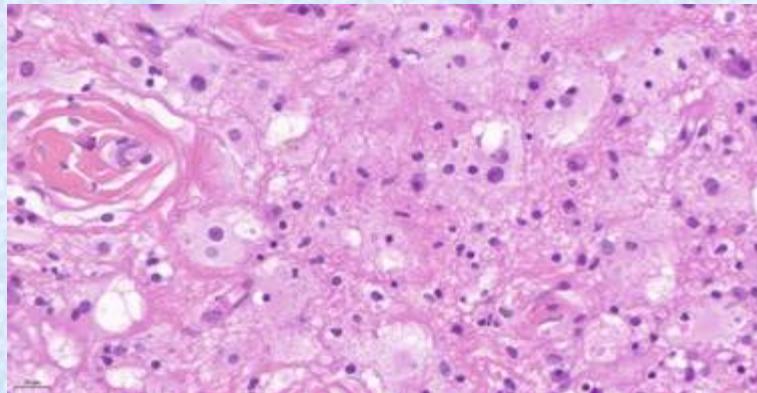
- Most adults with disseminated mixed (ECD, ICH and LCH) histiocytosis
- Most children with pure ICH limited to the skin

Rosai Dorfman disease (RDD): classical

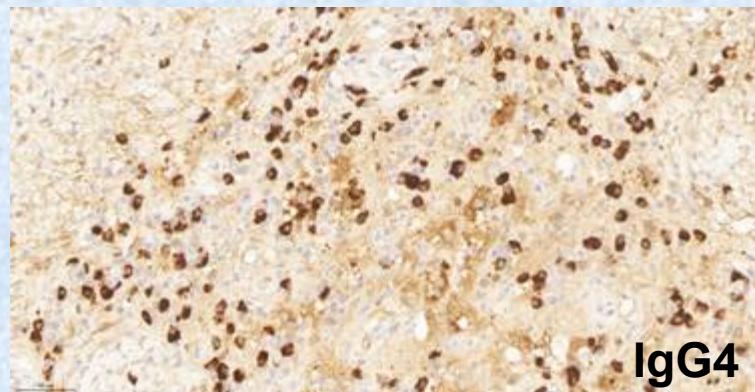
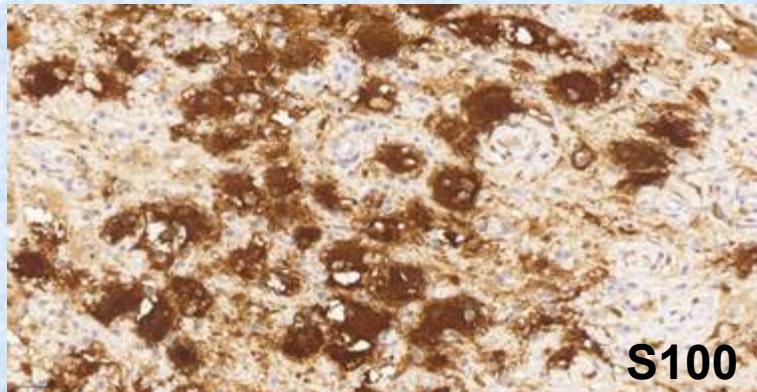


1 year old boy with cervical lymph nodes

RDD: overlapping diseases & emerging concepts



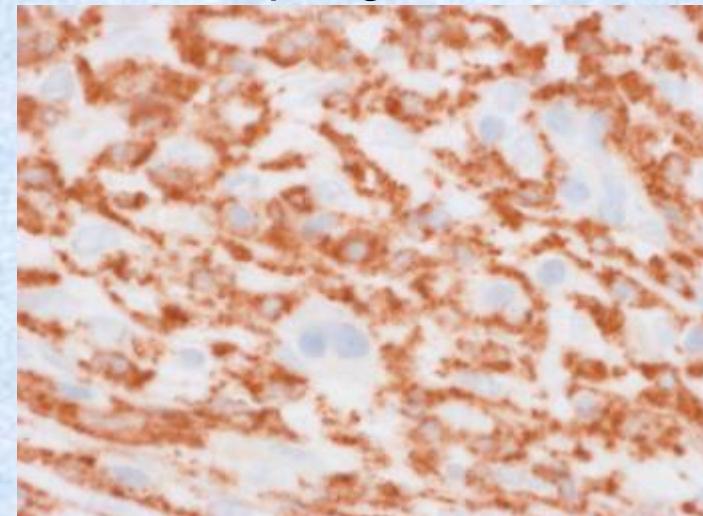
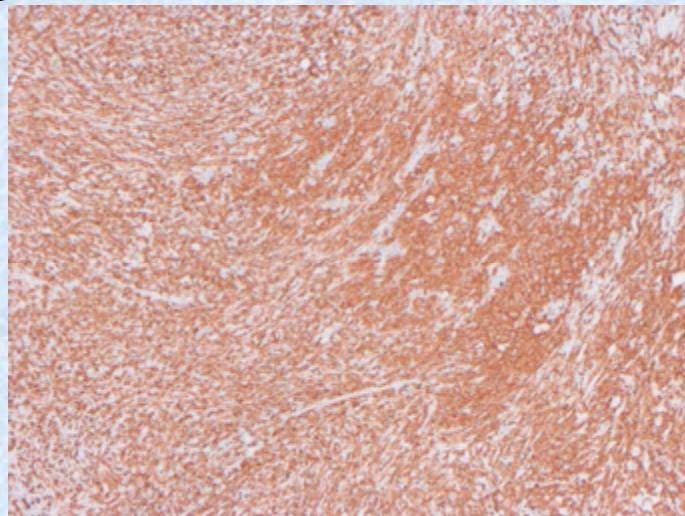
22 years old male
with pachymeningitis



- Inherited disease associated with increased RDD (*SLC29A3*, *TNFRSF6*)
- RDD IgG4-rich vs IgG4-related disease
- RDD histology in patients with typical ECD (or LCH)
- RDD with mutations activating the MAPkinase pathway (→ group L?)

Malignant Histiocytoses (MH)

- More than half of referred cases are not MH, but malignant tumors with abundant reactive macrophages



- Diagnosis is based on histology in an appropriate clinical context
- About one third of MH are secondary to pre-existing hemopathy; mainly ALL in pediatry and lymphomas in adults

Conclusion

- Intérêts de la relecture systématique centralisée
 - Sécurité diagnostique
 - Confrontations en RCP nationale histiocytoses
 - Formations (www.marih.fr)
 - Etudes anatomo-cliniques
 - Entités émergentes ou chevauchantes
- Intérêts de l'analyse moléculaire systématique centralisée
 - Spécificités / tumeurs solides
 - Techniques sensibles ciblées, panels dédiés
 - Accès à PFGM2025 (congélation)
- CRB (Biopsies, Sang, ADN, ARN)
 - Recherches translationnelles
 - Physiopathogénie (progéniteurs hématopoïétiques, etc...)
 - Nouvelles mutations / Sensibilité aux inhibiteurs
 - Biomarqueurs diagnostiques, pronostiques, théranostiques
 - Evolution des concepts, des critères diagnostiques et de la nosologie

Remerciements

- Pathologistes, membres du groupe de relecture :
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A Idbaih, A Tazi,
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