Inflammation et Cancer

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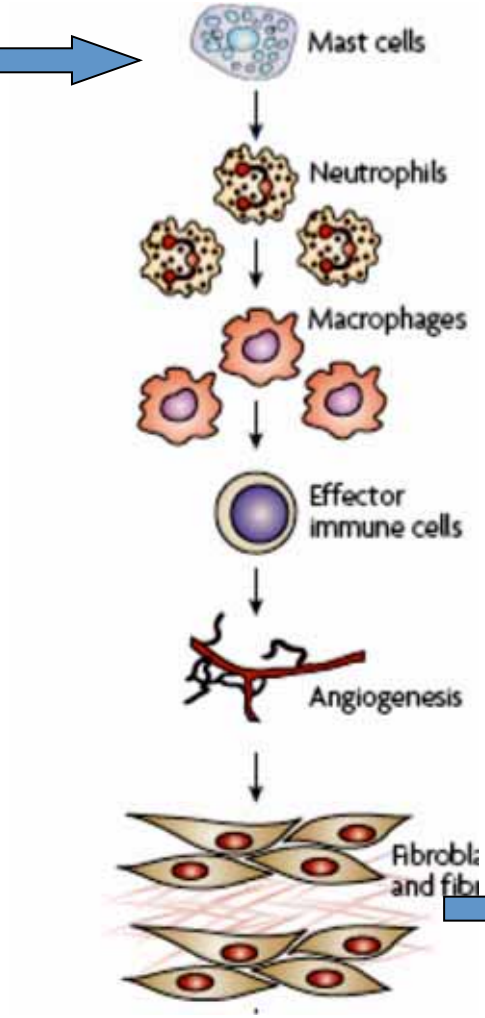
Que se passe t-il au cours de l'inflammation « simple »?

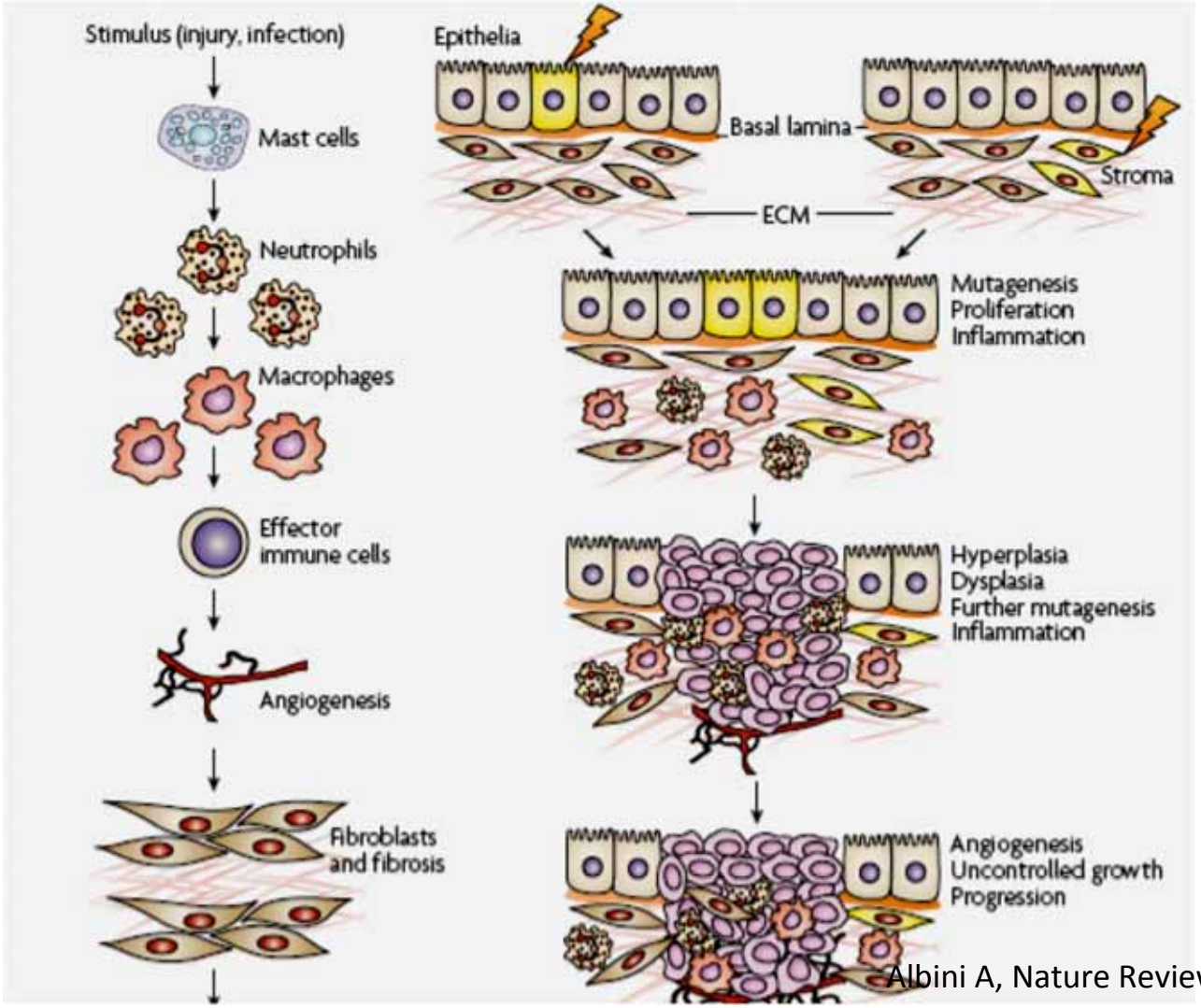
Stimulus :
agression, infection



Remodelage

Albini A, Nature Reviews Cancer 2007

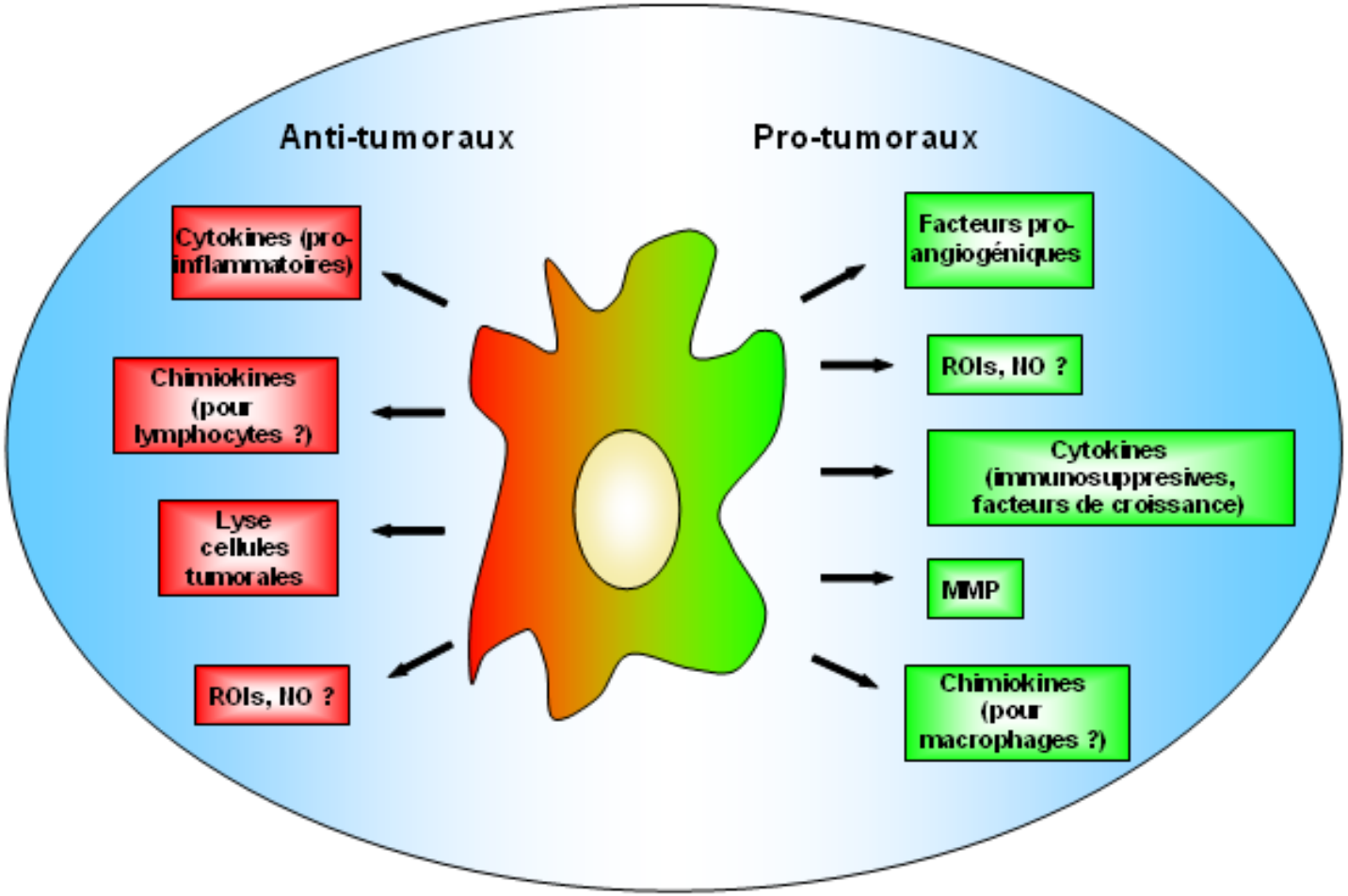
Que se passe t-il au cours du cancer ?



Albini A, Nature Reviews Cancer 2007

Inflammation et cancer :

dualité des cellules inflammatoires



Inflammation et cancer :

épidémiologie

Inflammation et cancer :
épidémiologie

Inflammatory bowel disease (colon cancer)

Helicobacter pylori (gastric cancer)

Chronic viral hepatitis (liver cancer)

Schistosome infection (bladder and colon)

Human Papilloma Virus (cervical cancer)

EBV (Burkitts lymphoma and nasopharyngeal cancer)

Cigarette smoking (lung cancer)

Immunité et cancer :
épidémiologie

- **Immunosurveillance anti-tumorale**
  - augmentation de l'incidence des cancers en cas d'immunosuppression
    - acquise : greffés, SIDA
    - congénitale : déficit immunitaire commun variable
  - rôle pronostique de l'infiltration intra tumorale des lymphocytes et des cellules NK

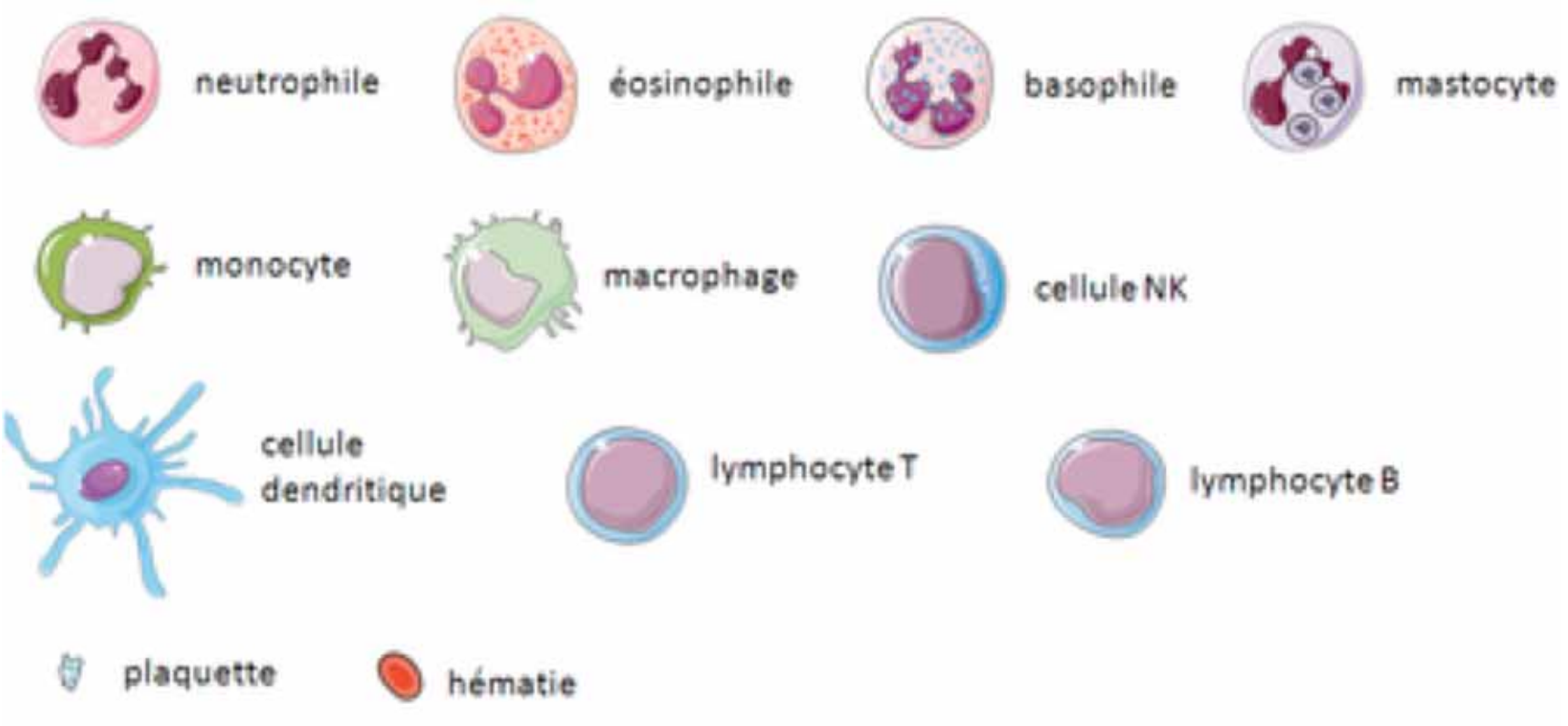
Lymphocytes T et cancer

L'infiltration cellulaire lymphocytaire T est de bon pronostic

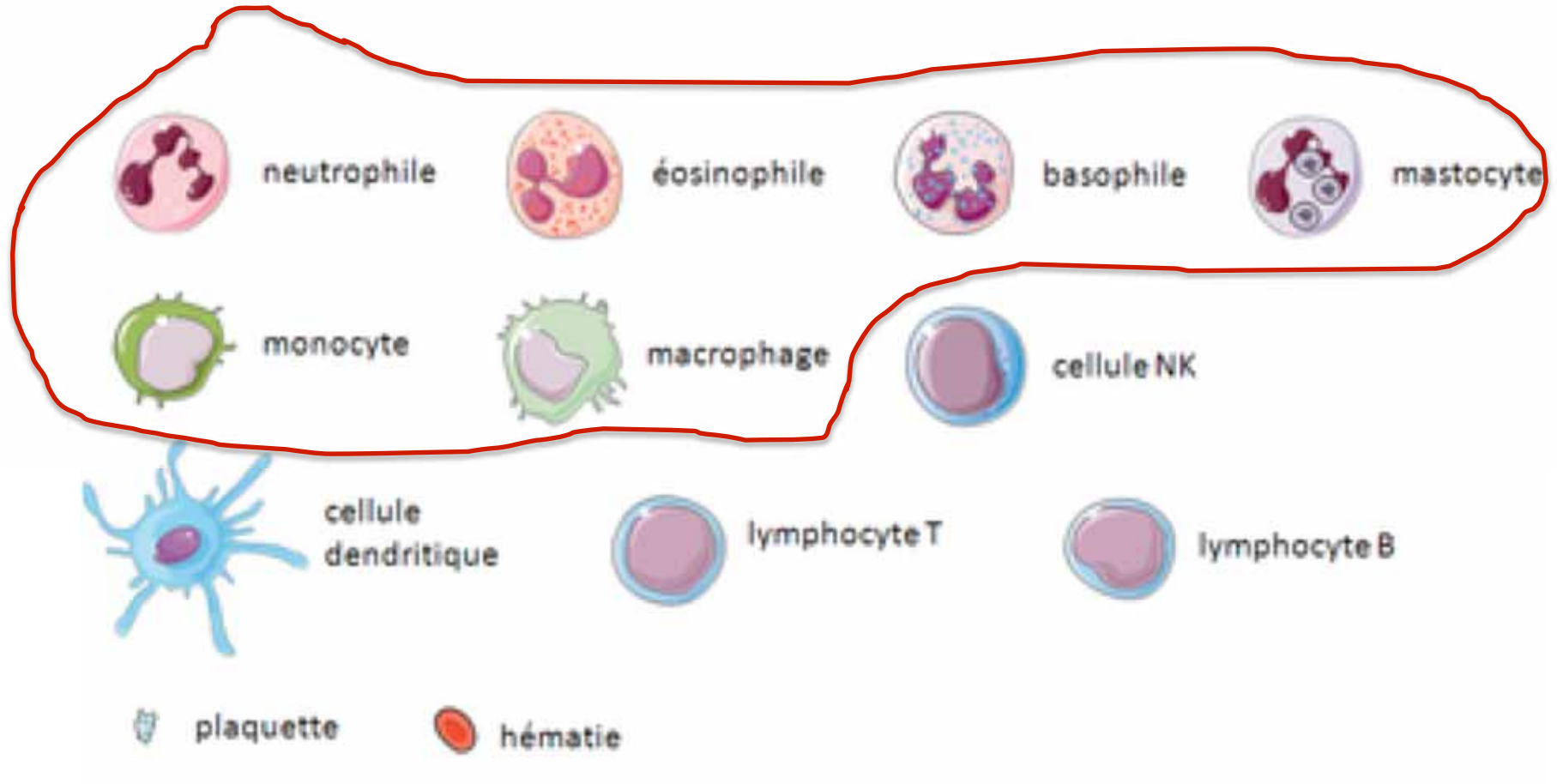
Cancers	*References*
Melanoma	Clark *et al.* (1989); Tefany *et al.* (1991); Mackensen *et al.* (1993); Clemente *et al.* (1996)
Head and neck cancers	Reichert *et al.* (2001); Shibuya *et al.* (2002); Badoual *et al.* (2006)
Breast cancer	Marrogi *et al.* (1997); Menegaz *et al.* (2008)
Bladder cancer	Sharma *et al.* (2007)
Ovarian cancer	Zhang *et al.* (2003); Sato *et al.* (2005)
Esophageal cancer	Schumacher *et al.* (2001); Cho *et al.* (2003)
Colorectal cancer	Jass (1986); Graham and Appelman (1990); Harrison *et al.* (1994); Ropponen *et al.* (1997); Baier *et al.* (1998); Naito *et al.* (1998); Dalerba *et al.* (2003); Diederichsen *et al.* (2003); Prall *et al.* (2004); Pages *et al.* (2005, 2009); Galon *et al.* (2006); Salama *et al.* (2009)
Renal cell carcinoma	Nakano *et al.* (2001)
Prostatic adenocarcinoma	Vesalainen *et al.* (1994); Karja *et al.* (2005); Richardsen *et al.* (2008)
Lung carcinoma	Ito *et al.* (2005); Hiraoka *et al.* (2006a); Al-Shibli *et al.* (2008); Dieu-Nosjean *et al.* (2008); Kawai *et al.* (2008)

Pages et al. Oncogene 2010

Inflammation et cancer : types cellulaires

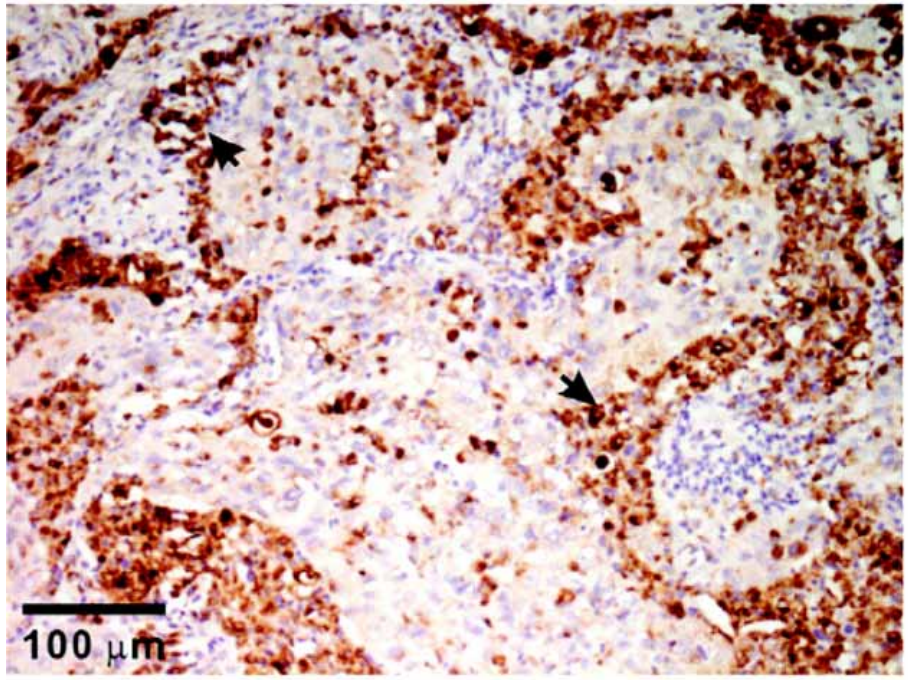


Inflammation et cancer : types cellulaires

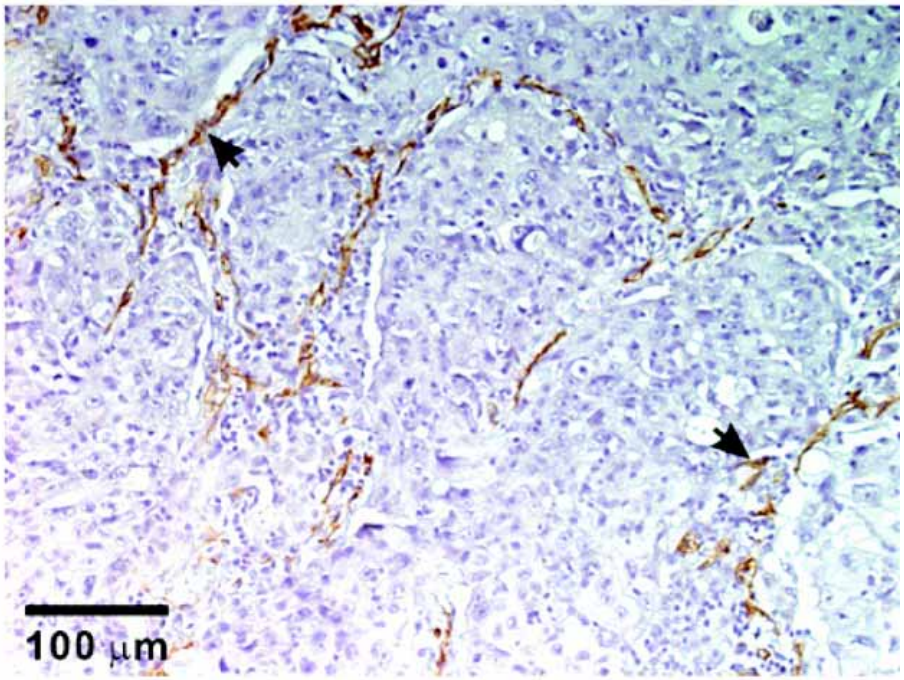


Inflammation et cancer : *macrophages*

macrophages



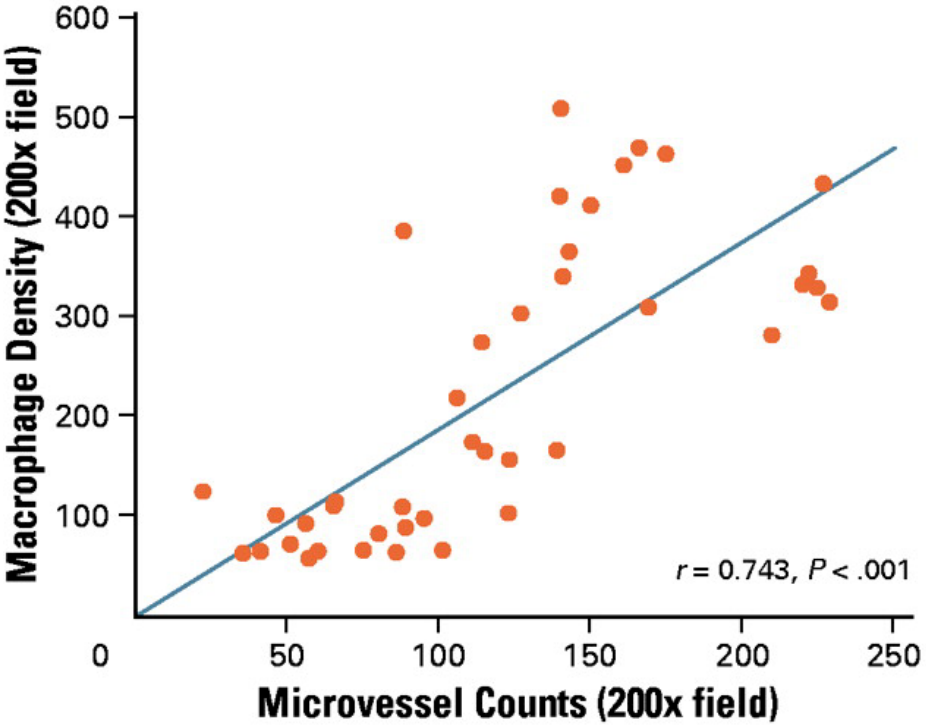
microvaisseaux

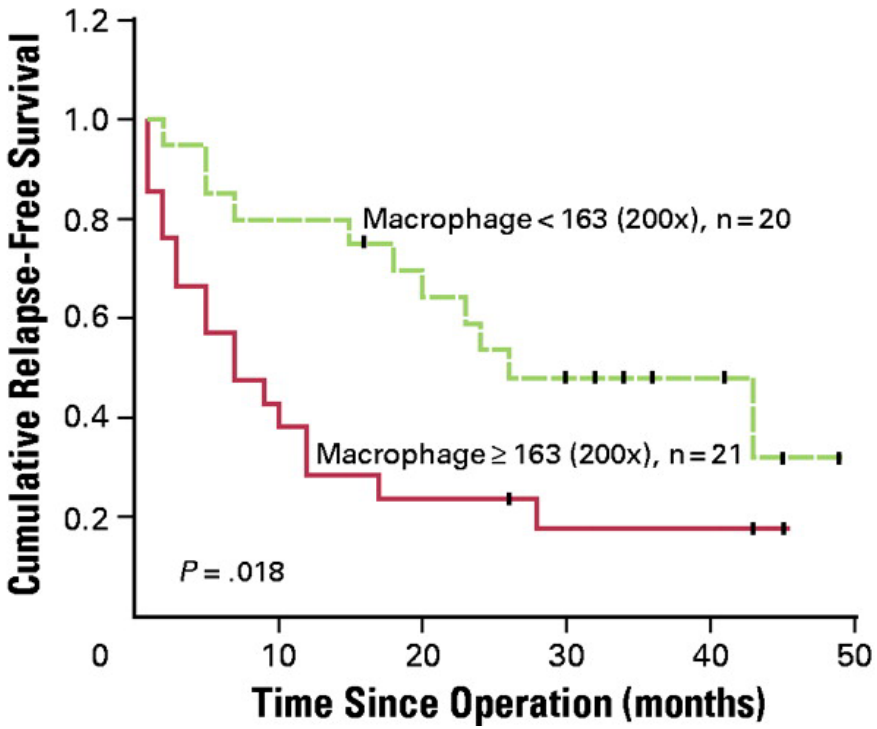


Chen JJ, J Clin Oncol 2005

Macrophages et cancer :

microvaisseaux et pronostic

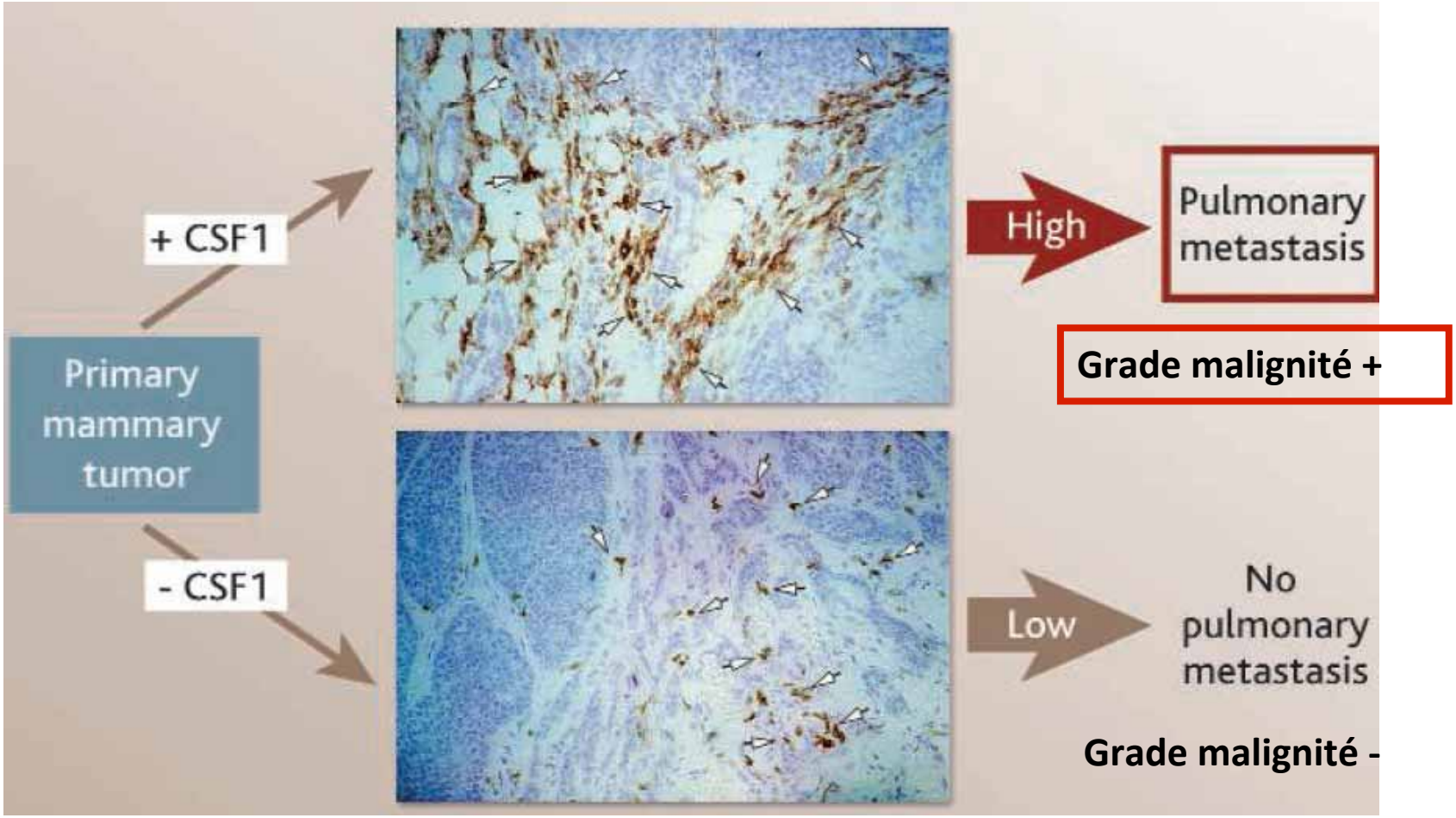




Chen JJ, J Clin Oncol 2005

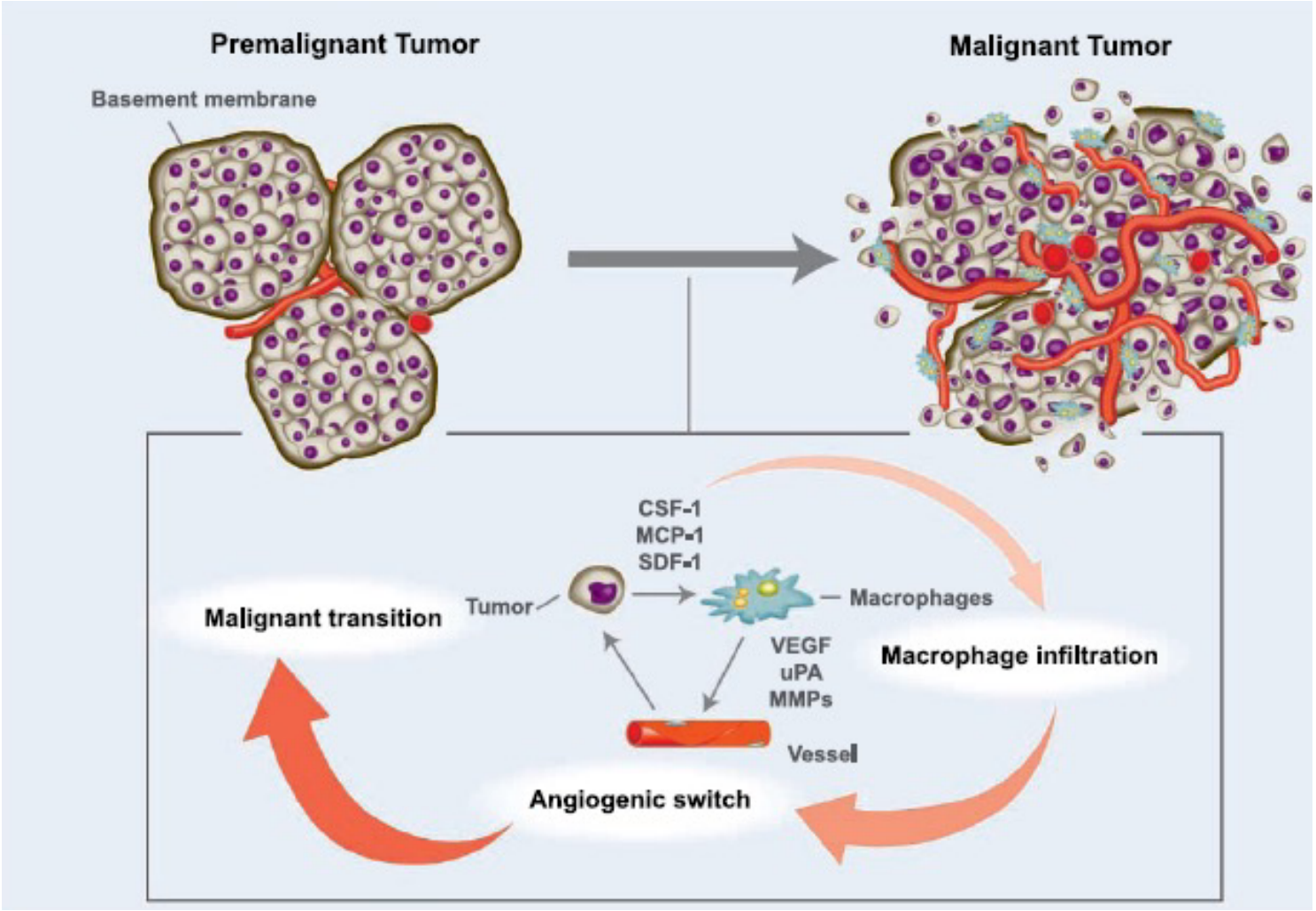
Macrophages et cancer :

le switch angiogenique



Marx J, Science 2004

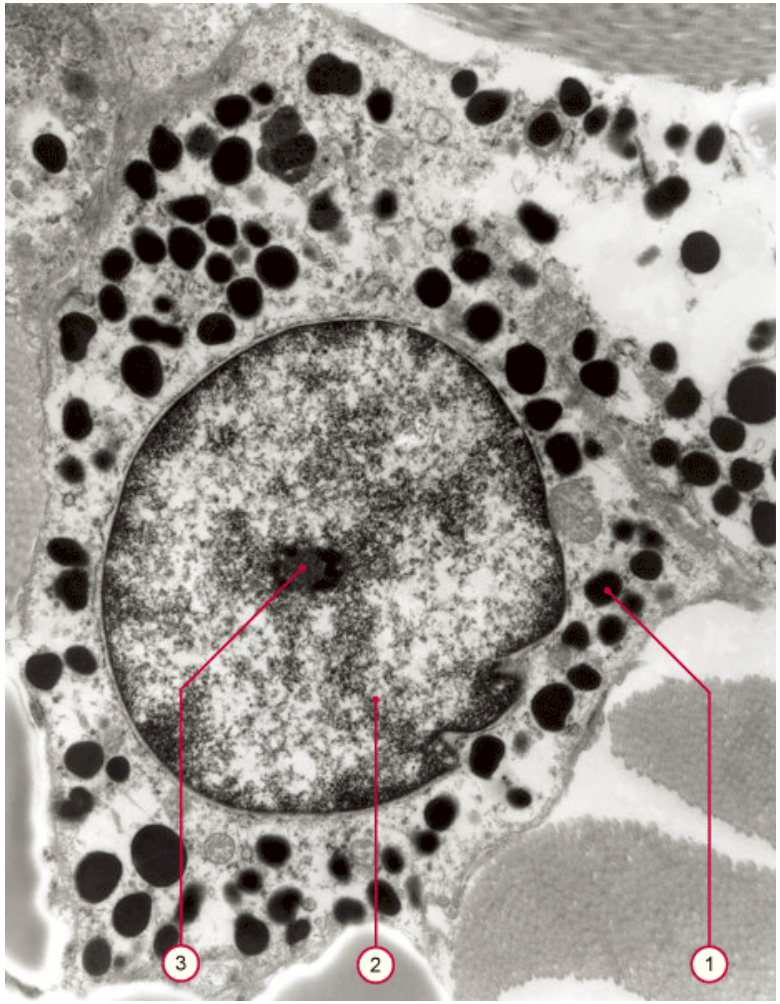
Macrophages et cancer :
le switch angiogenique

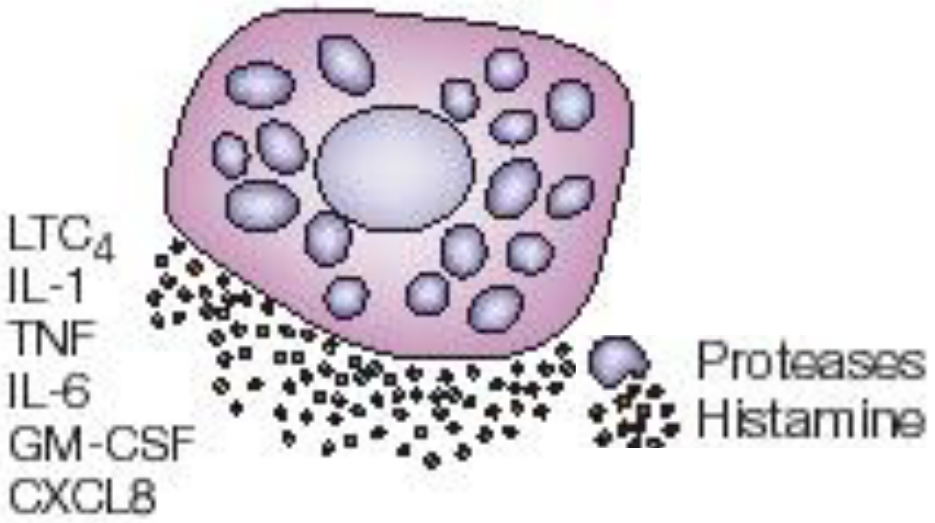


Lin E, Cancer Res 2007

Inflammation et cancer :

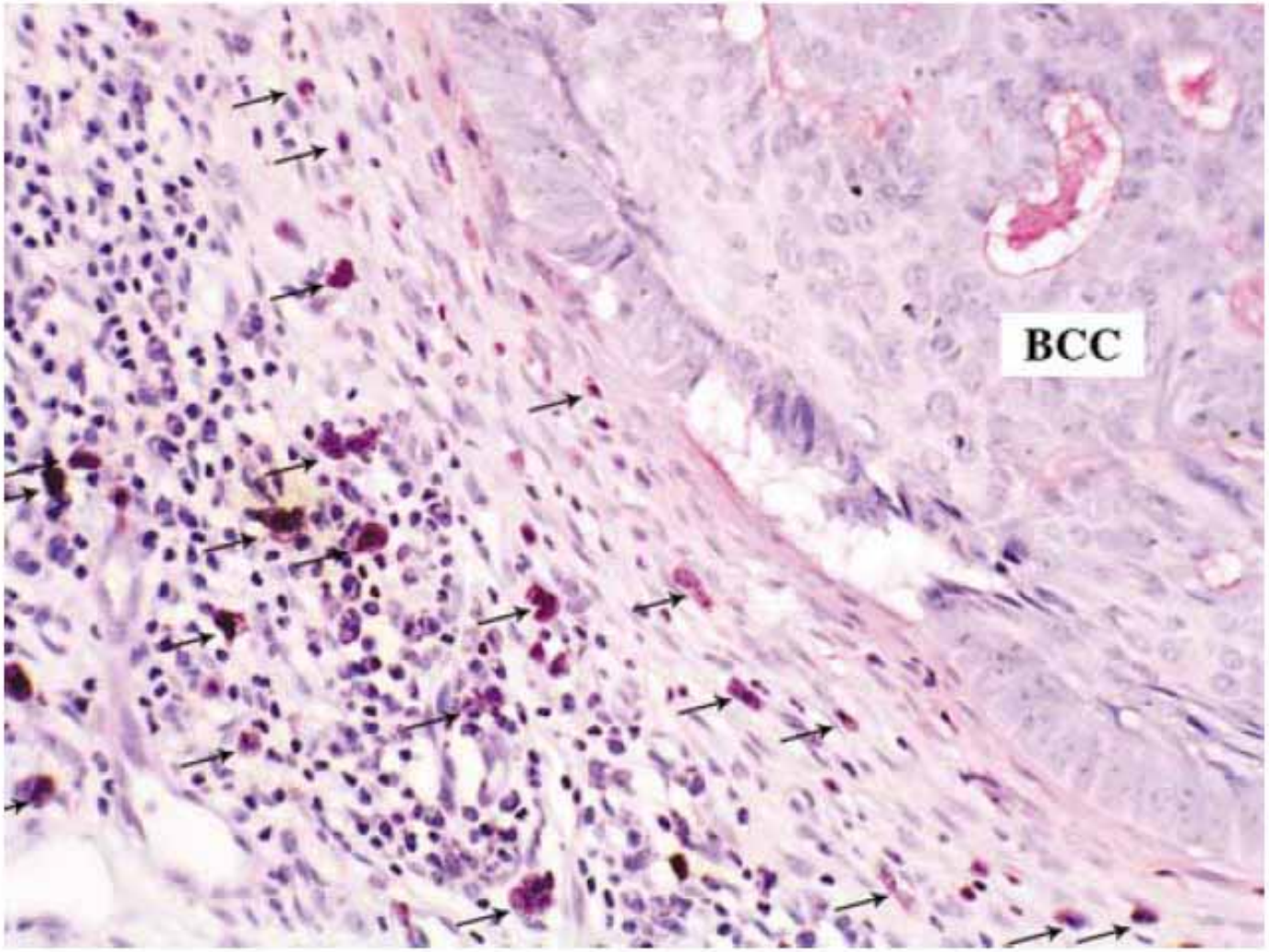
exemple : les mastocytes





Heparine
VEGF
FGF

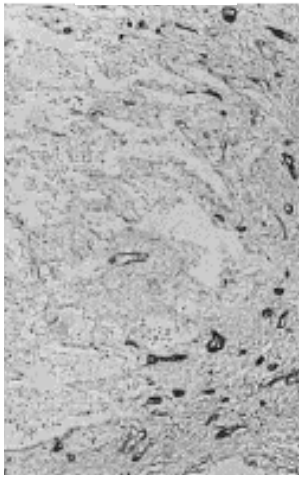
Mastocytes et cancer :

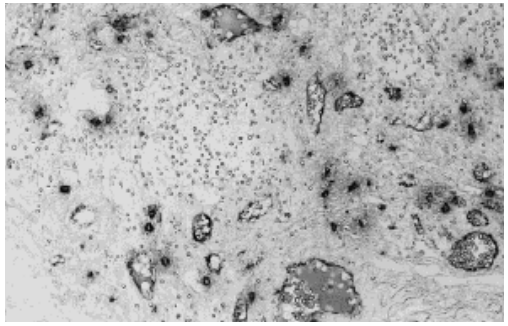


Mastocytes et cancer :

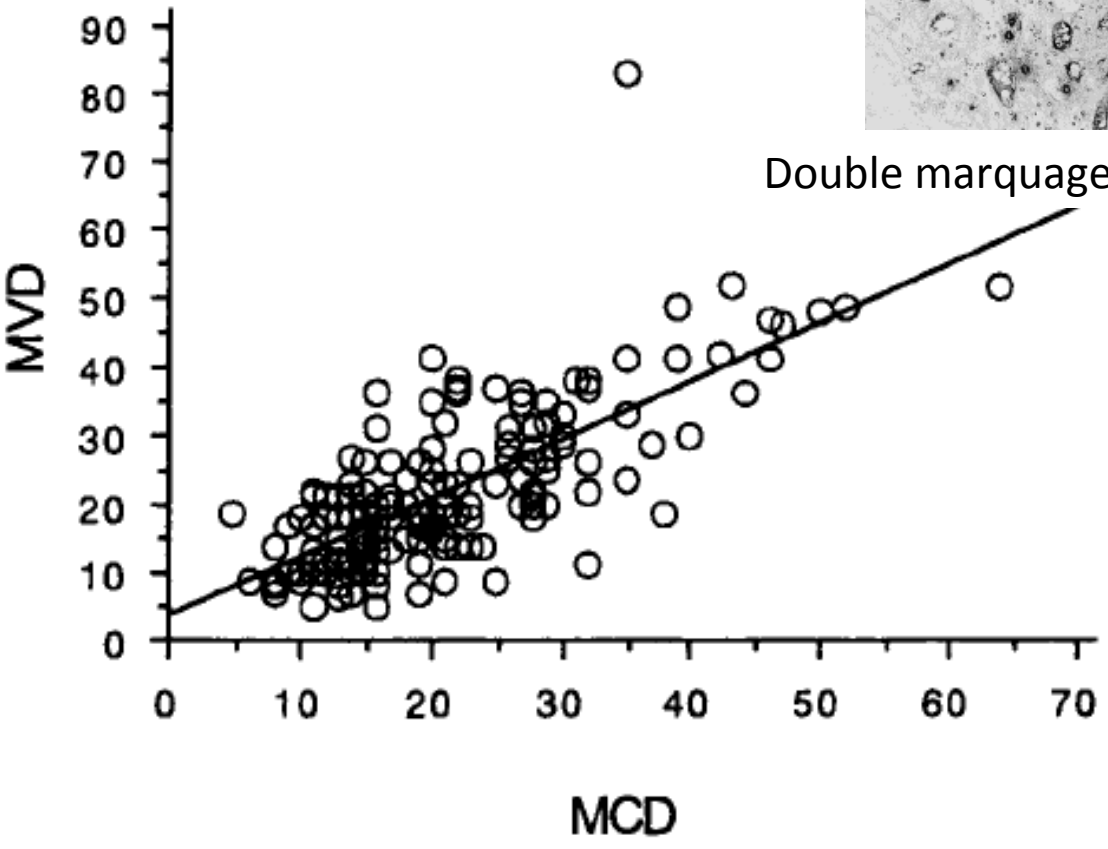
microvaisseaux

CD34

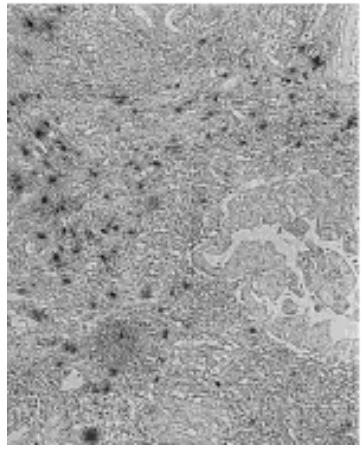




Double marquage tryptase CD34



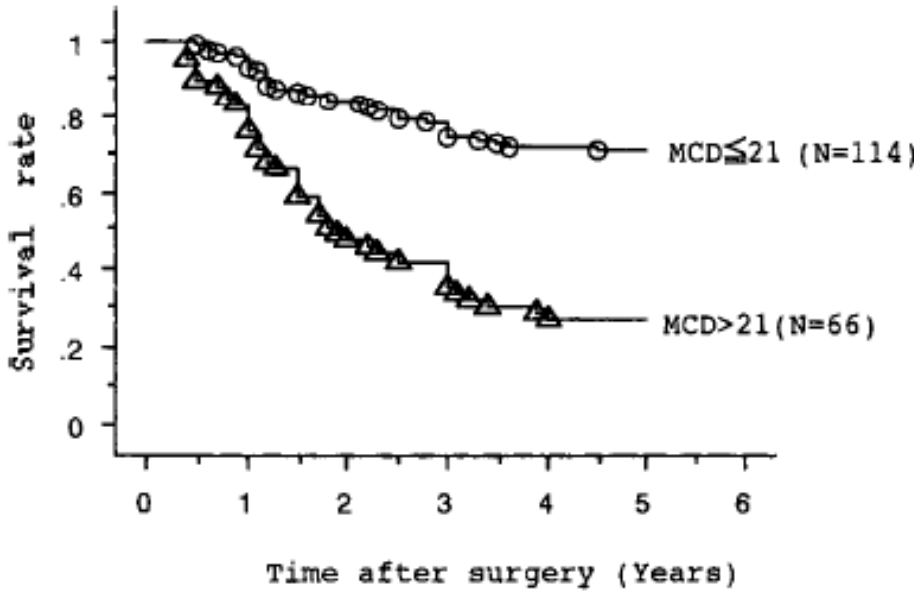
Tryptase

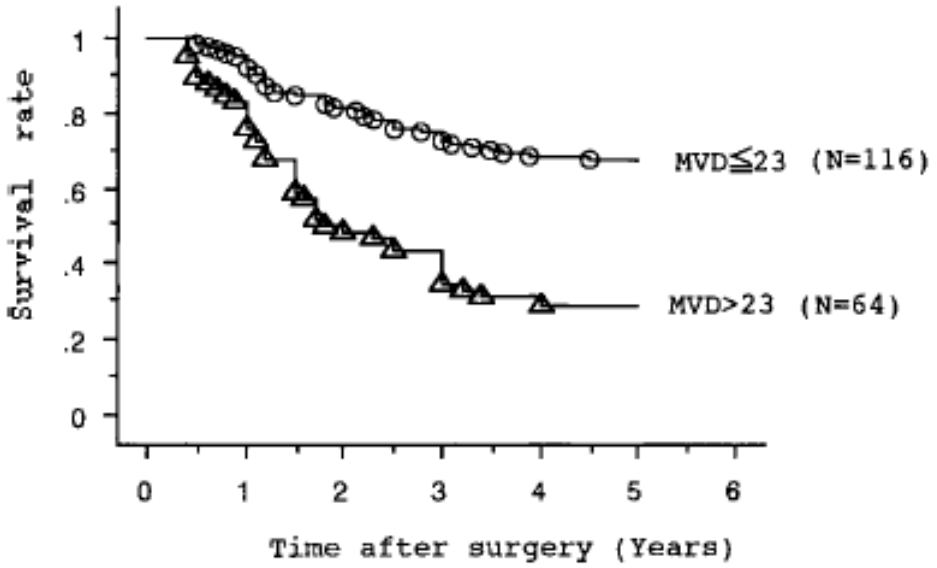


Takanami I, Cancer 2000

Mastocytes et cancer :

pronostic





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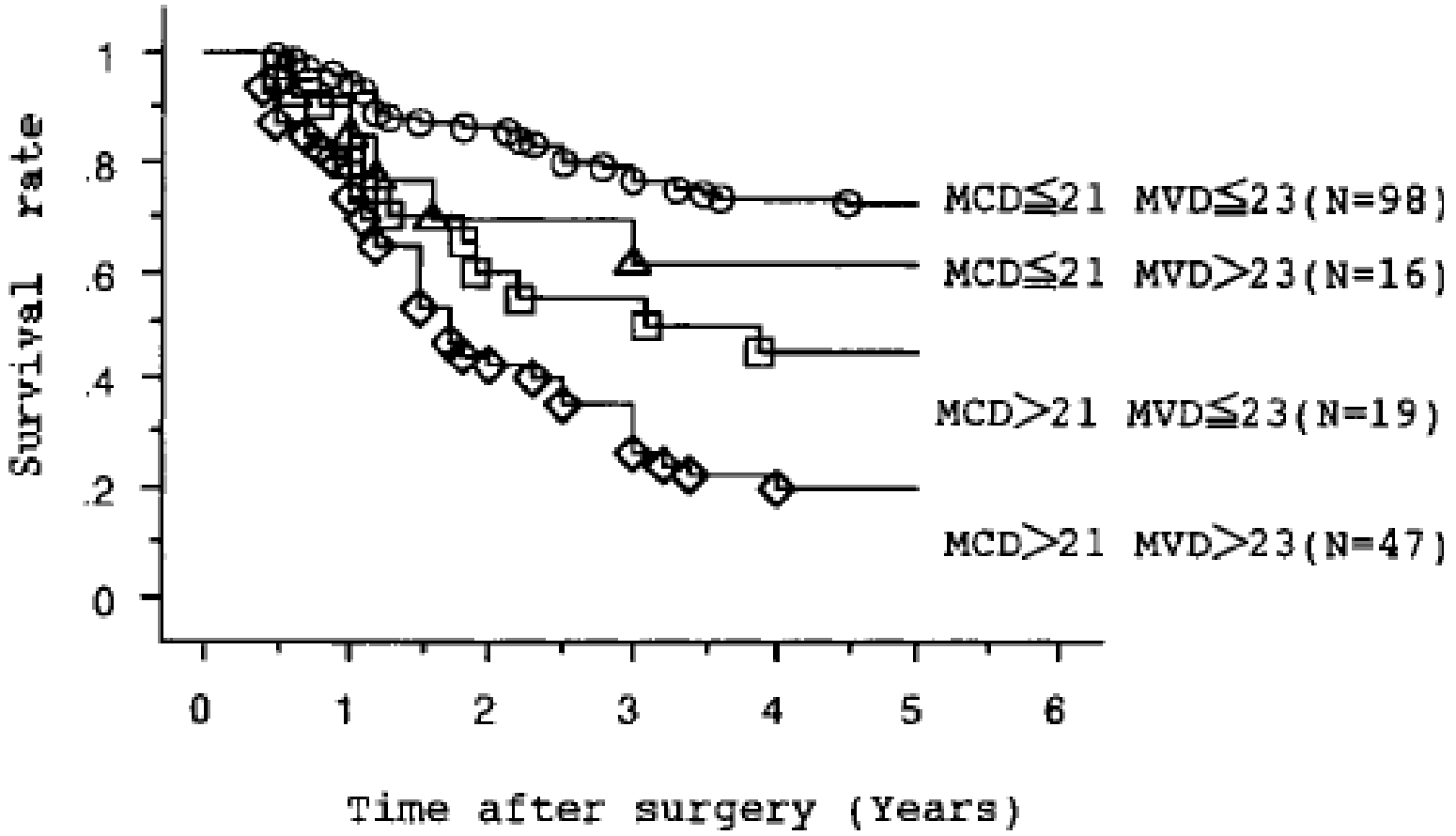
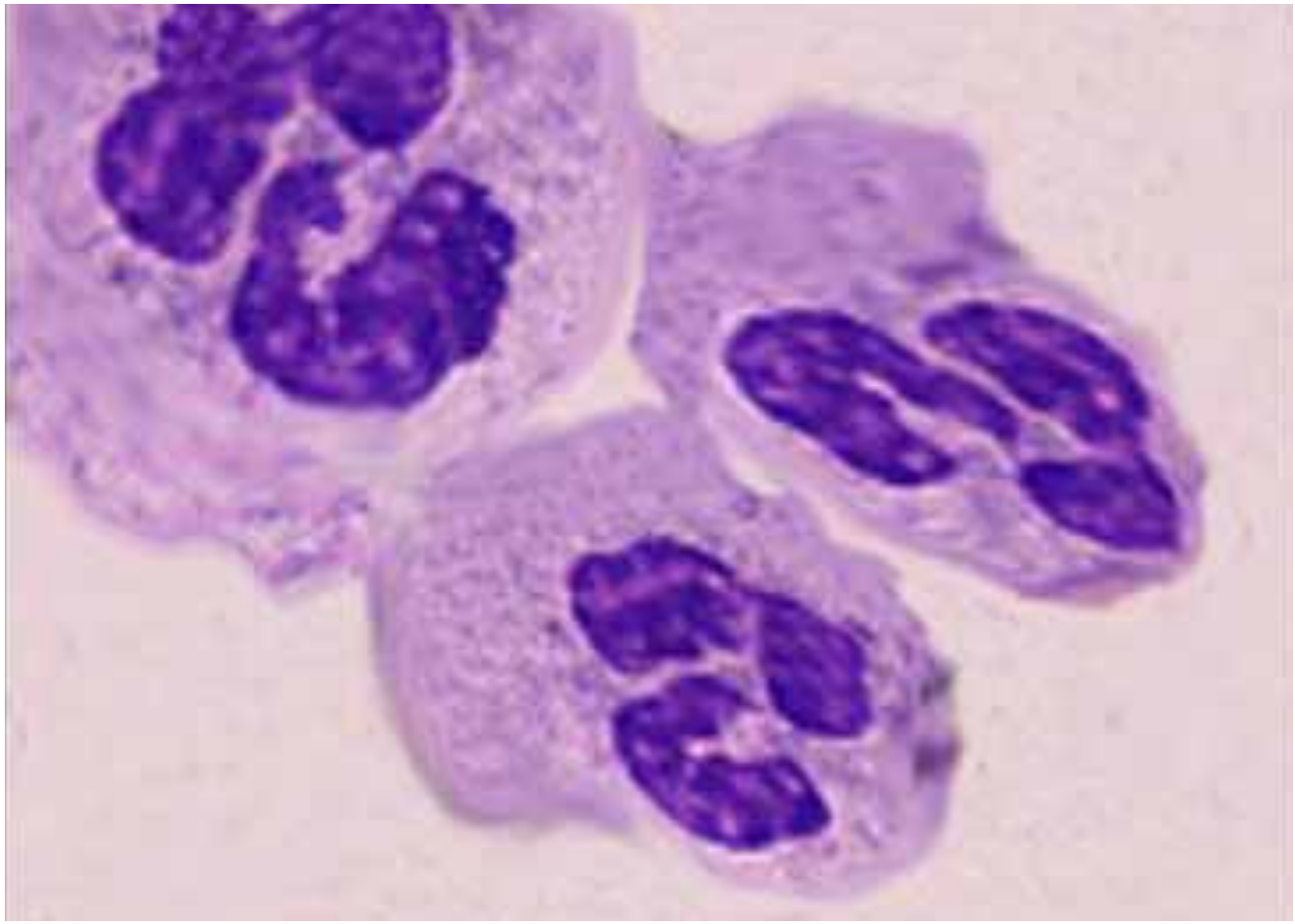


Takanami I, Cancer 2000

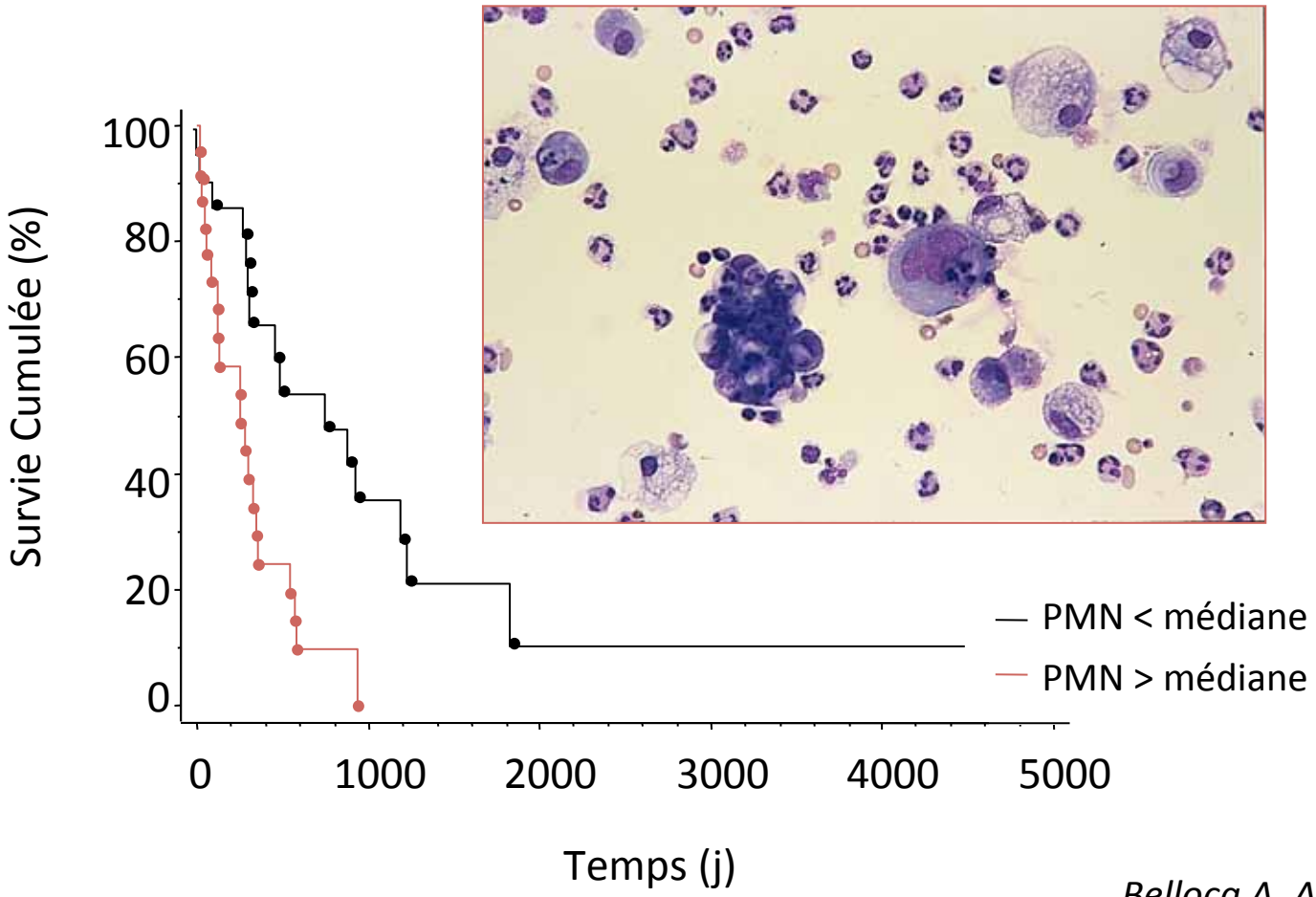
Inflammation et cancer :

neutrophiles



Inflammation et cancer :

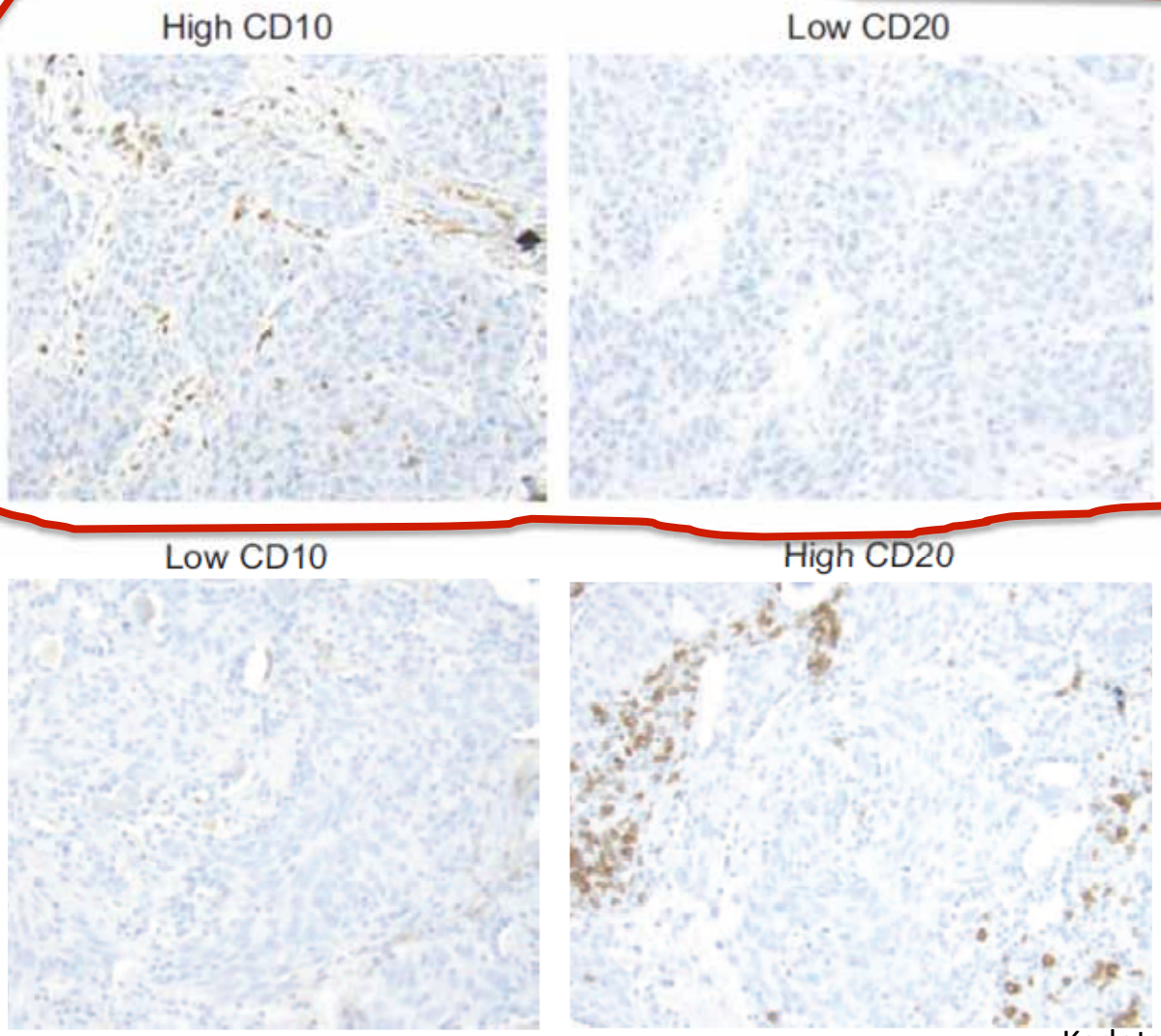
neutrophiles et progression aérogène



Bellocq A, Am J Pathol.1998

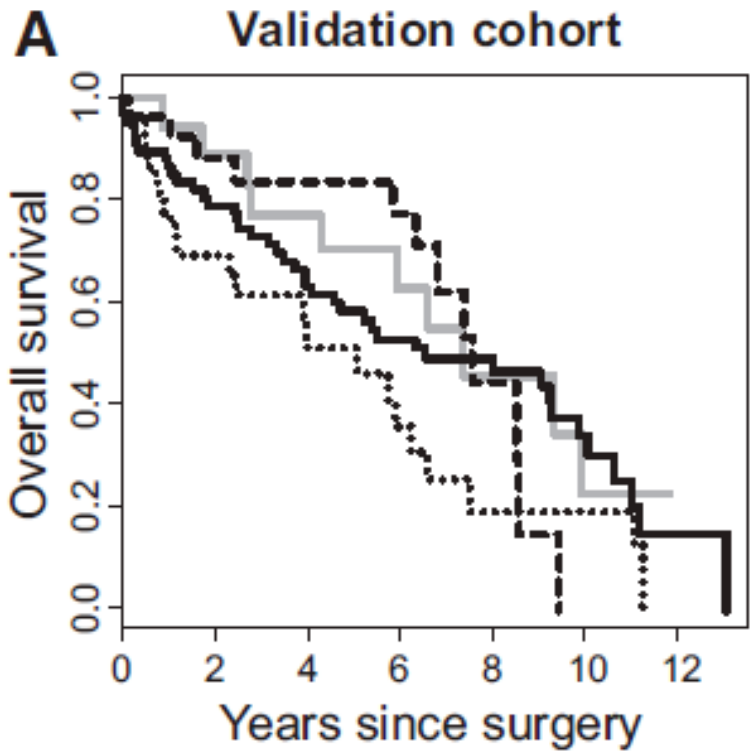
Neutrophiles et cancer :

ratio neutrophiles / lymphocytes

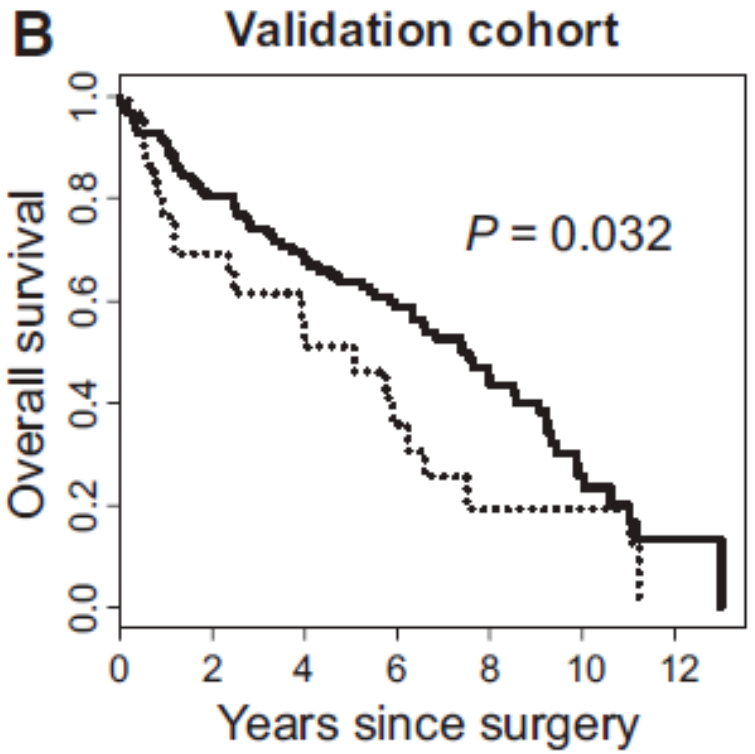


Kadota K, J Thorac Oncol 2015

Neutrophiles et cancer :
ratio neutrophiles / lymphocytes



	CD10/CD20	N	5-yr OS	*P*
———	low/low	67	58%	0.069
·····	high/low	30	46%	ref.
– – –	low/high	27	84%	0.10
———	high/high	18	71%	0.092



	CD10/CD20	Risk index	N	5-yr OS
———	others	low	112	66%
·····	high/low	high	30	46%

Kadota K, J Thorac Oncol 2015

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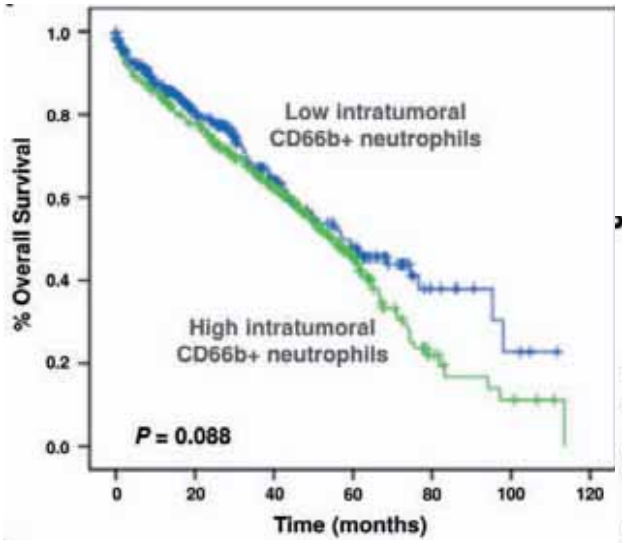
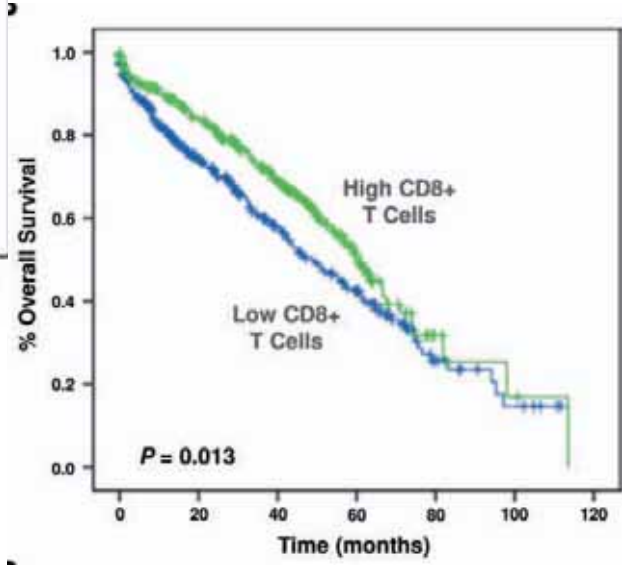
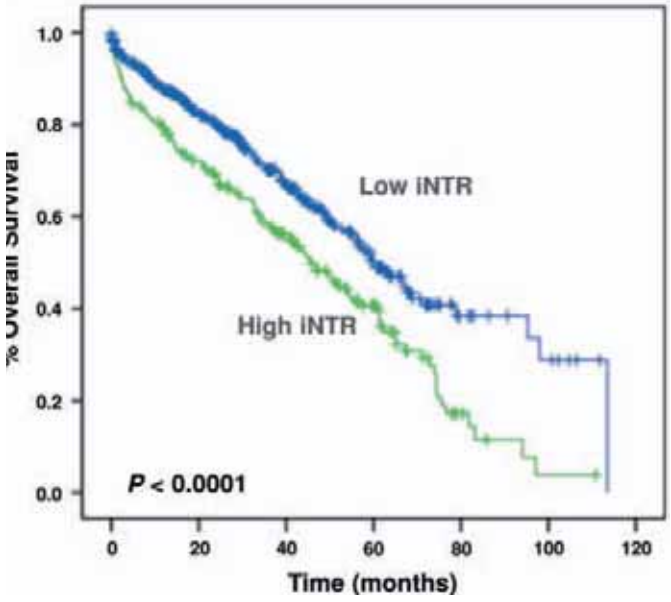
ratio neutrophiles / lymphocytes



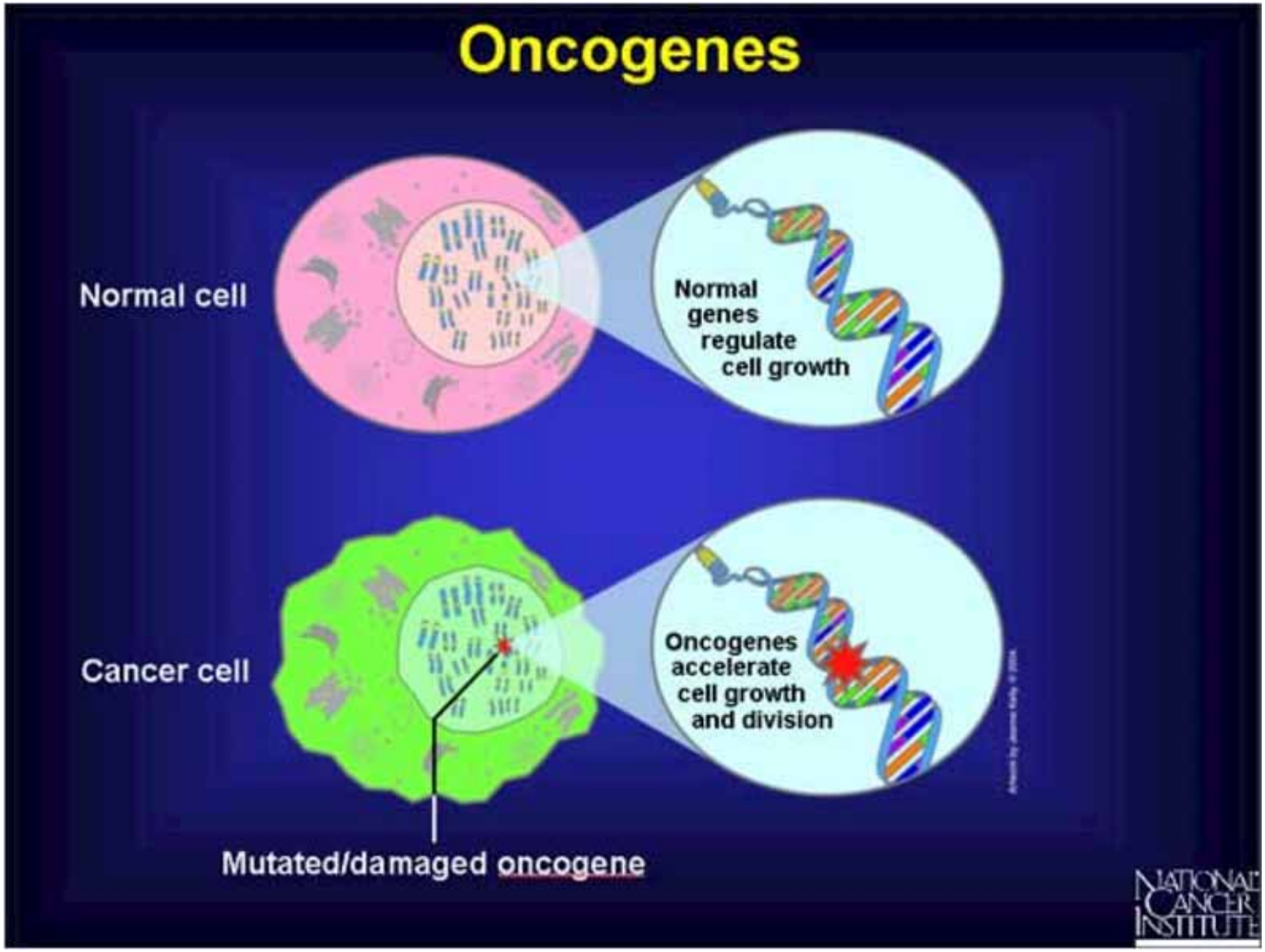




Ilie M, Cancer 2012

Inflammation et cancer :

épidémiologie

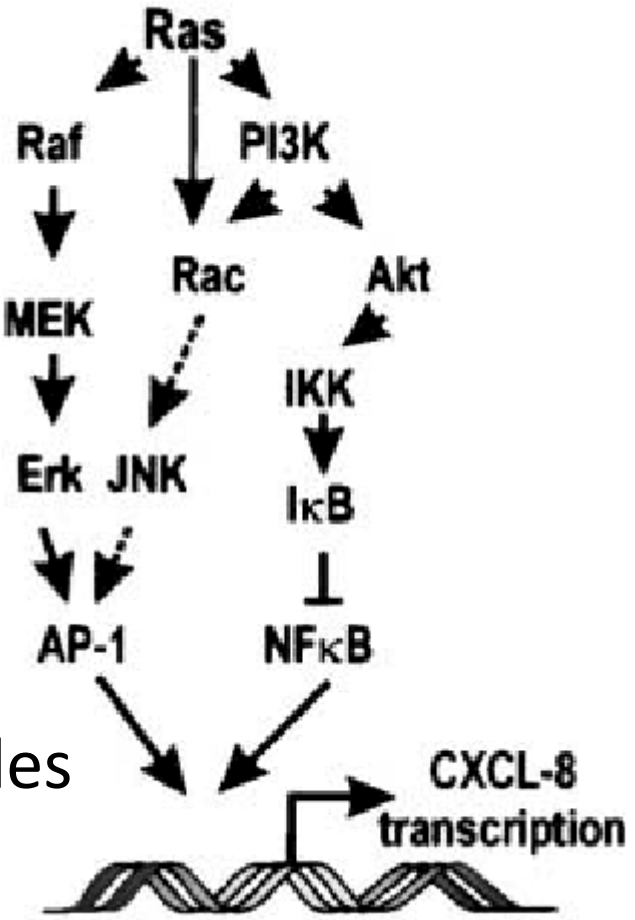


RAS et inflammation :
interleukine-8

L'activation de RAS stimule la transcription de l'interleukine-8

-proangiogenique

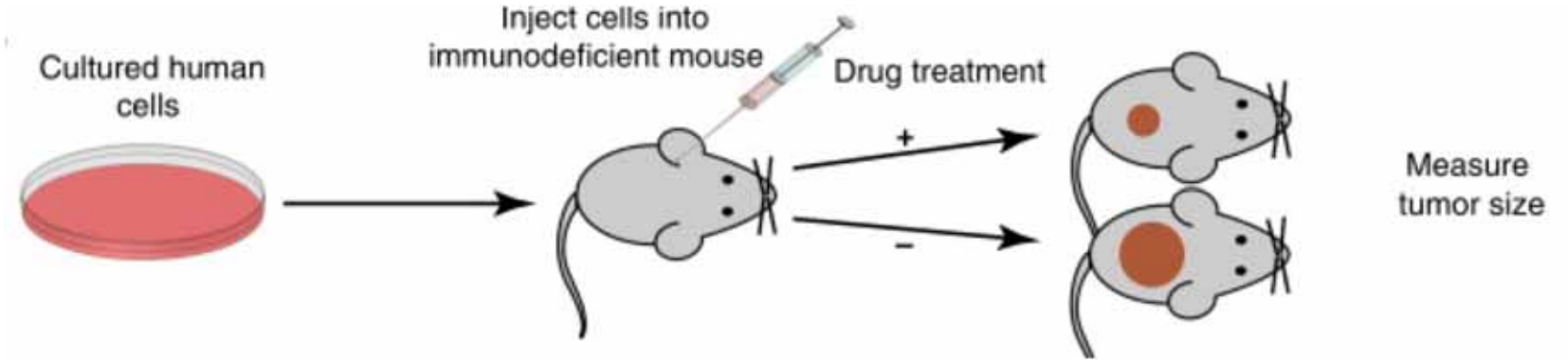
-chimiotactique pour les neutrophiles

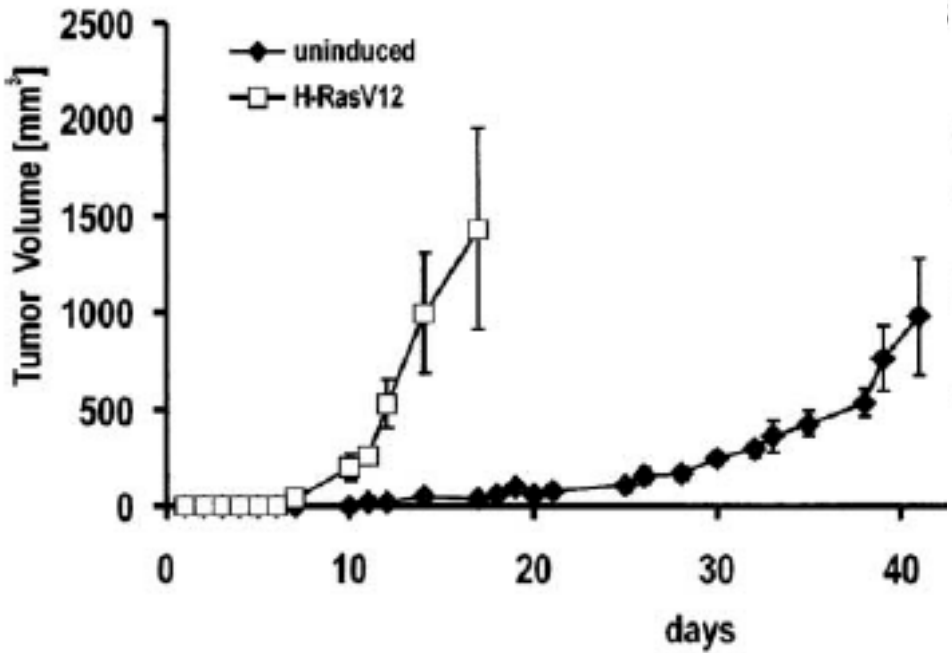


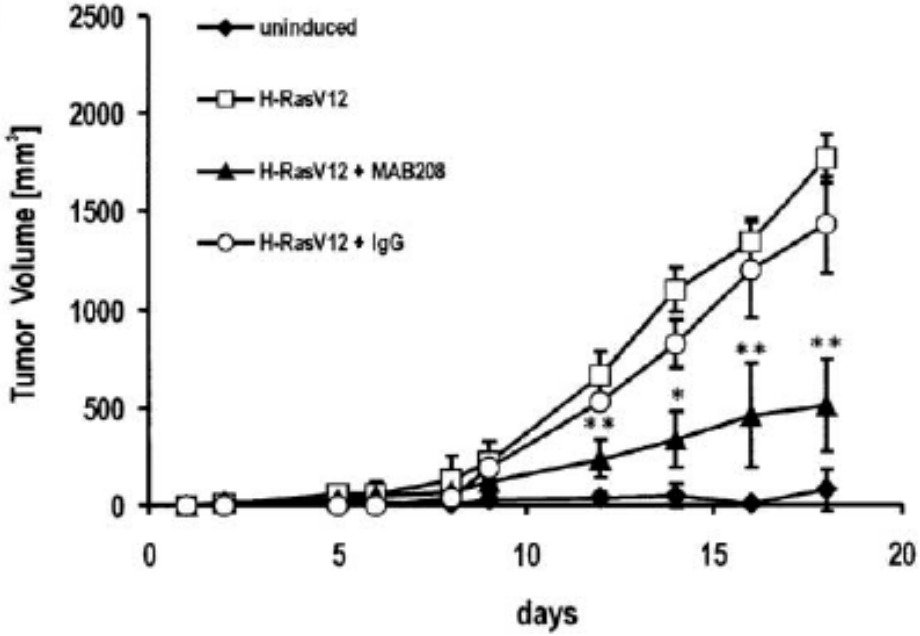
Sparmann A, Cancer Cell, 2004

Inflammation et cancer :

lignées mutées Ras et anti IL-8



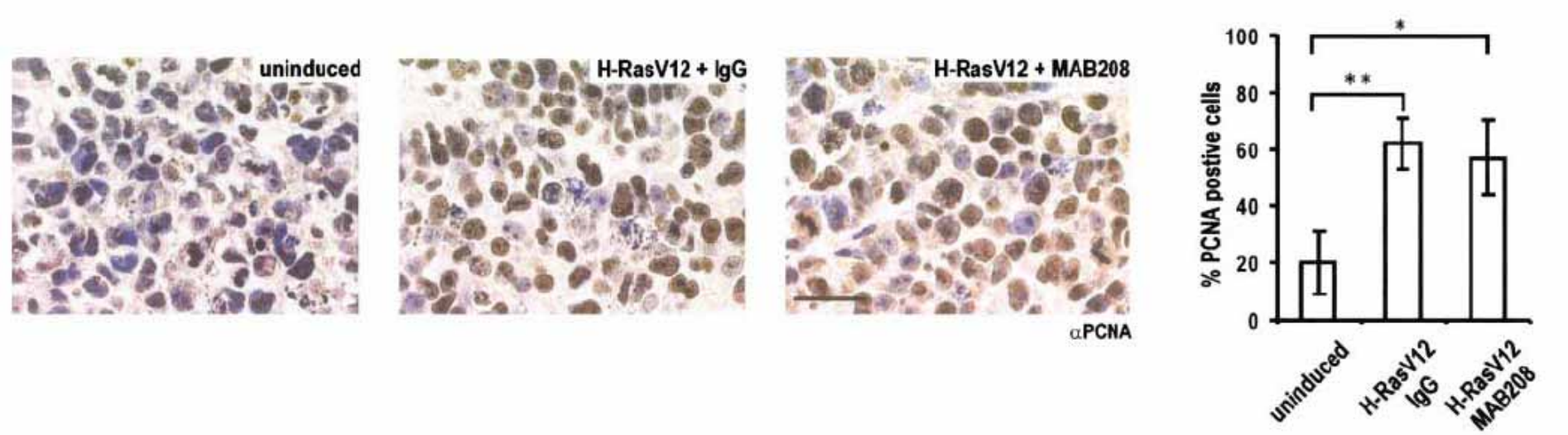




Sparmann A, Cancer Cell, 2004

Inflammation et cancer :

lignées mutées Ras et anti IL-8 prolifération?

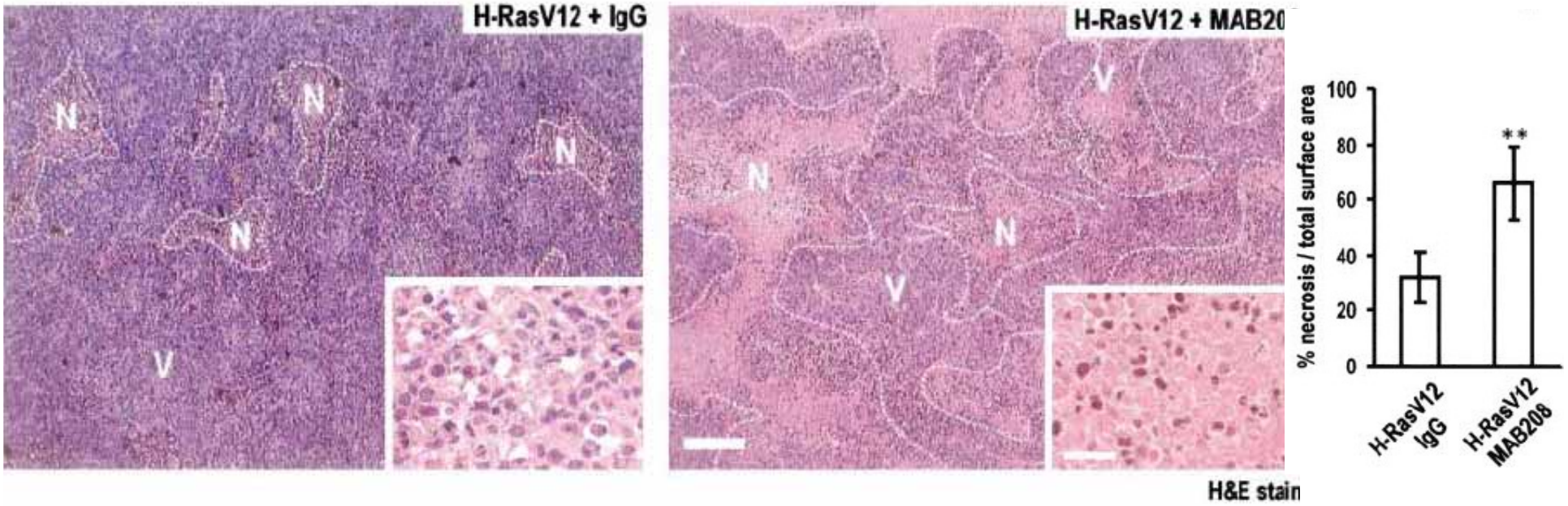


Sparmann A, Cancer Cell, 2004

Inflammation et cancer :

lignées mutées Ras et anti IL-8

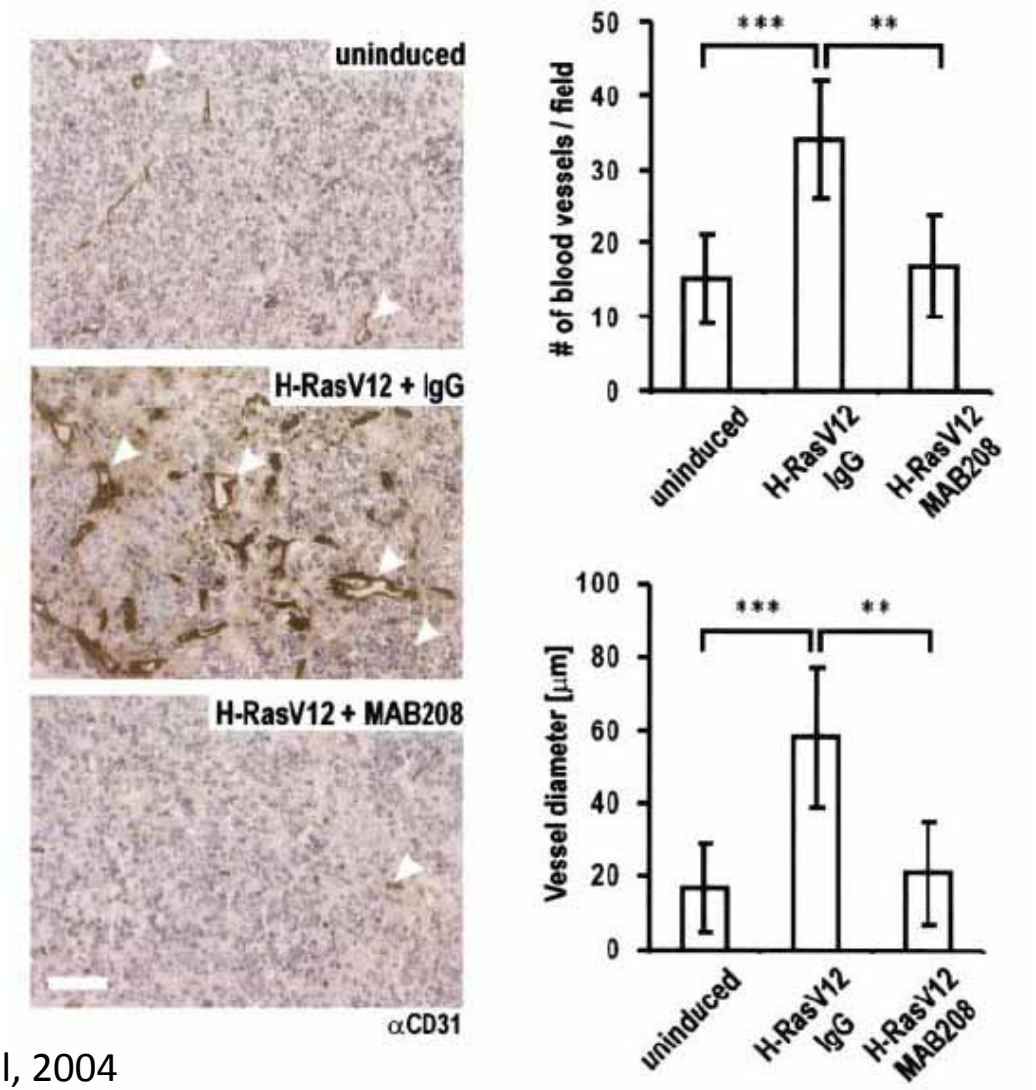
nécrose tumorale?



Sparmann A, Cancer Cell, 2004

Inflammation et cancer :

lignées mutées Ras et anti IL-8 angiogenèse?



Sparmann A, Cancer Cell, 2004

Inflammation et cancer :

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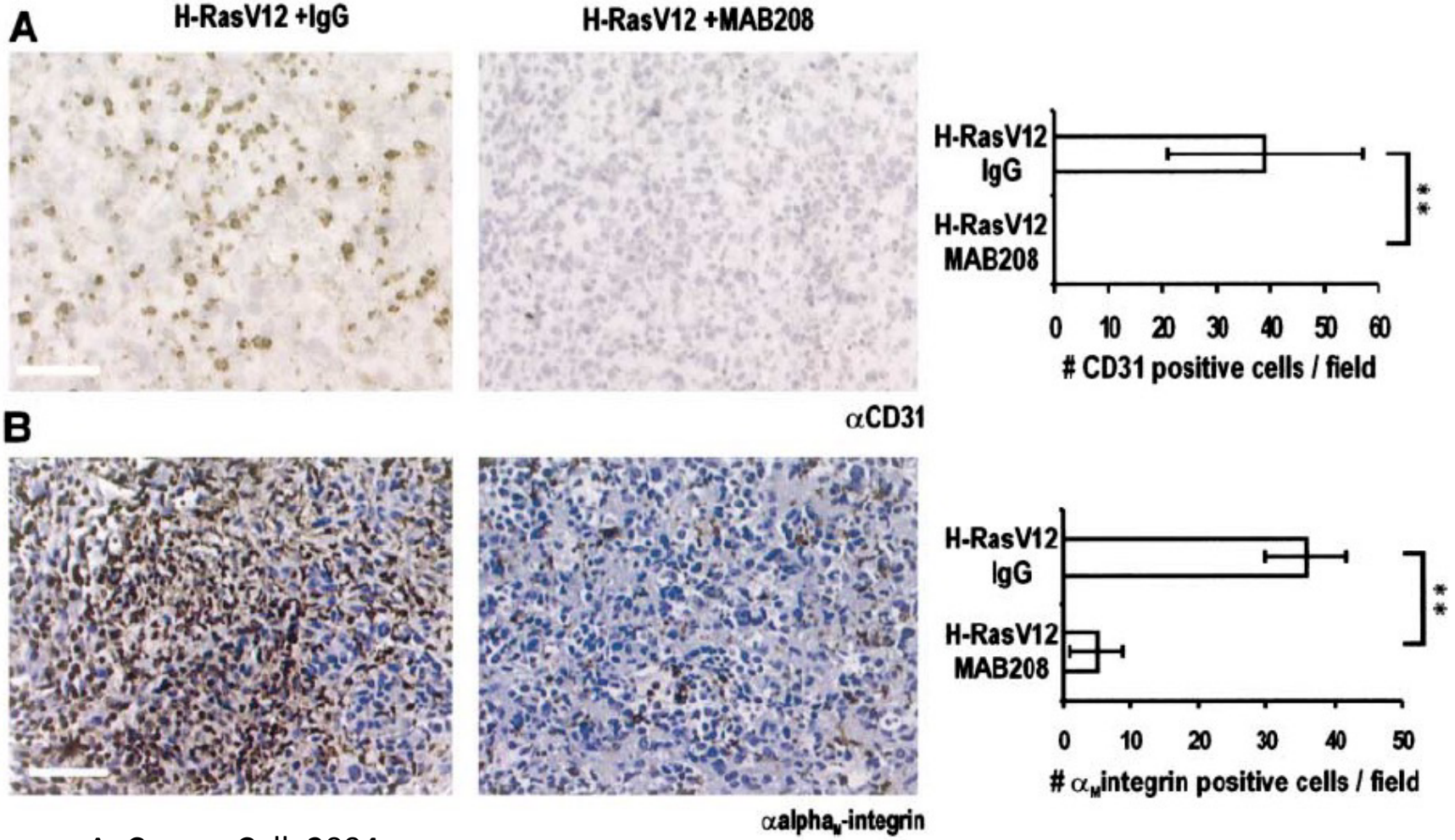
cellules myéloides?

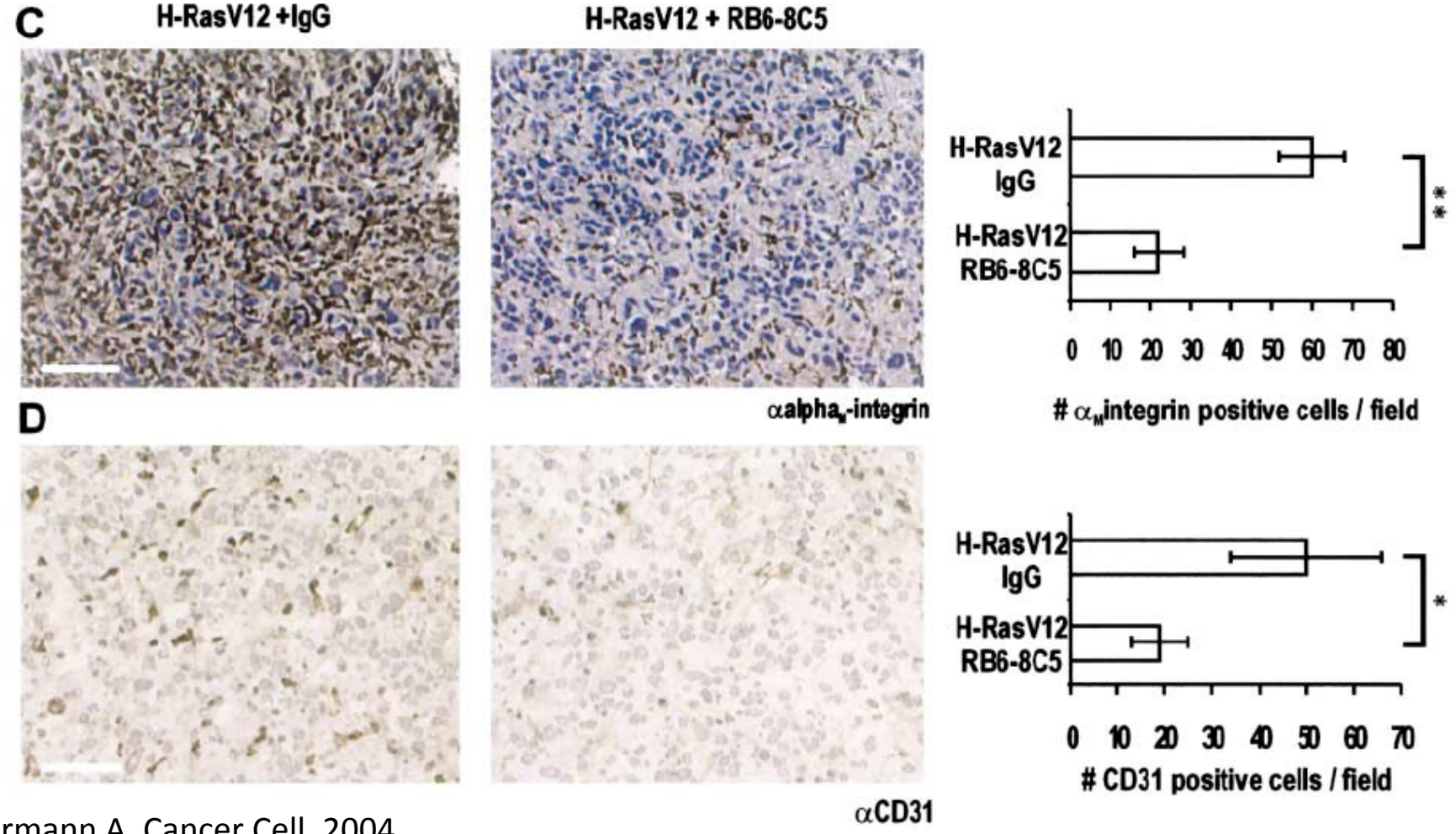


Sparmann A, Cancer Cell, 2004

Inflammation et cancer :

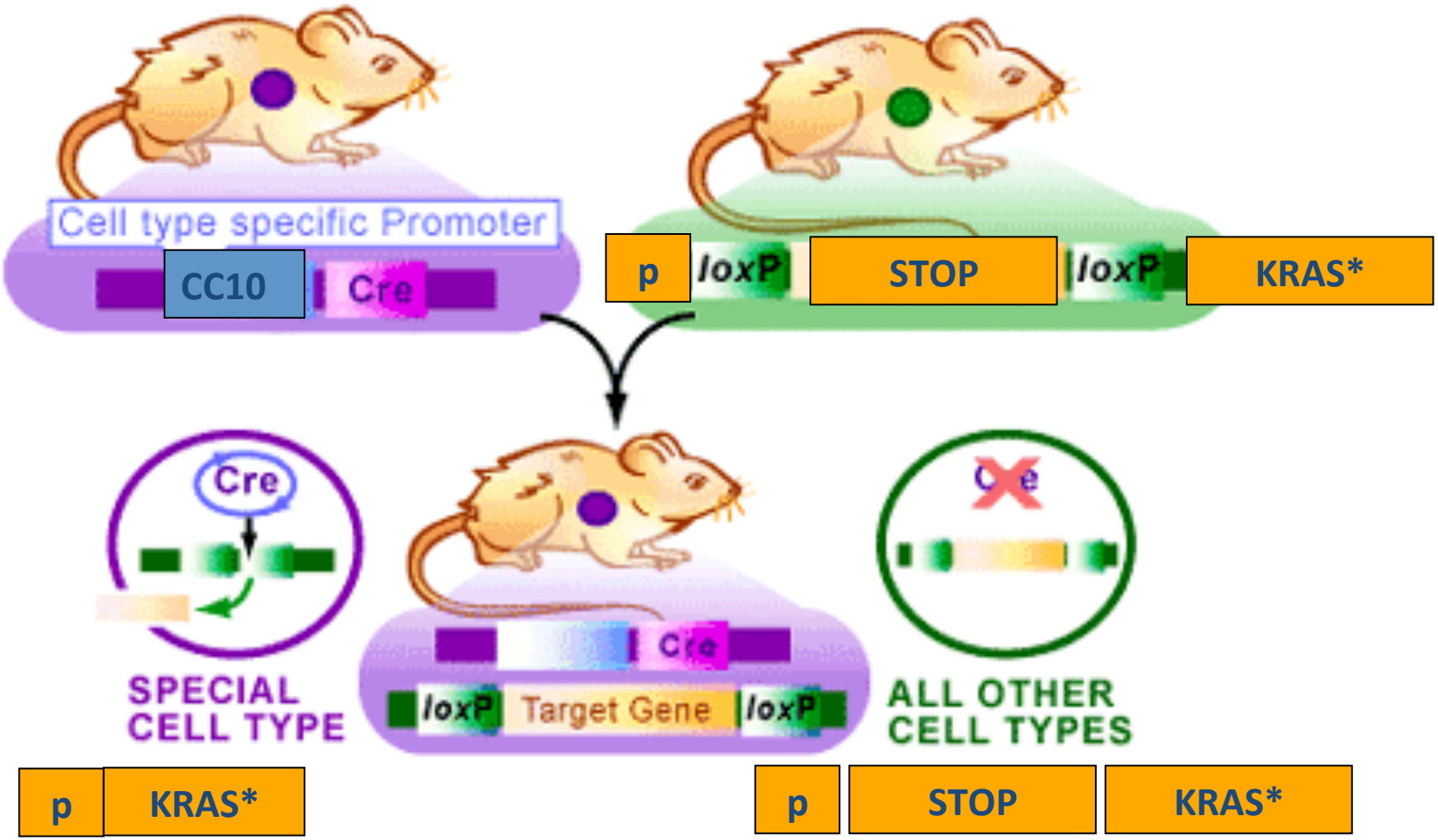
lignées mutées Ras et anti IL-8

déplétion en cellules myéloides?



Sparmann A, Cancer Cell, 2004

Modèle CC10-Cre/LSL-K-ras

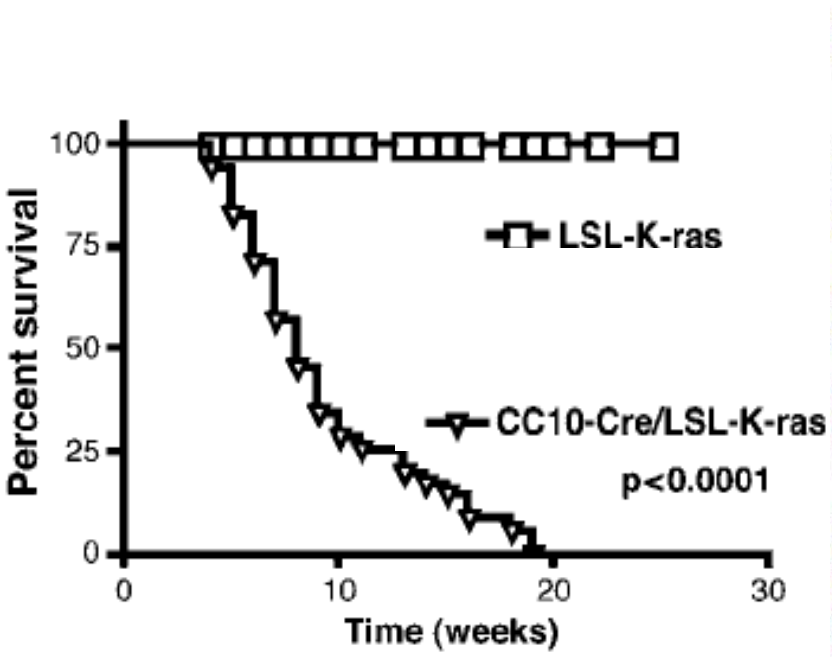


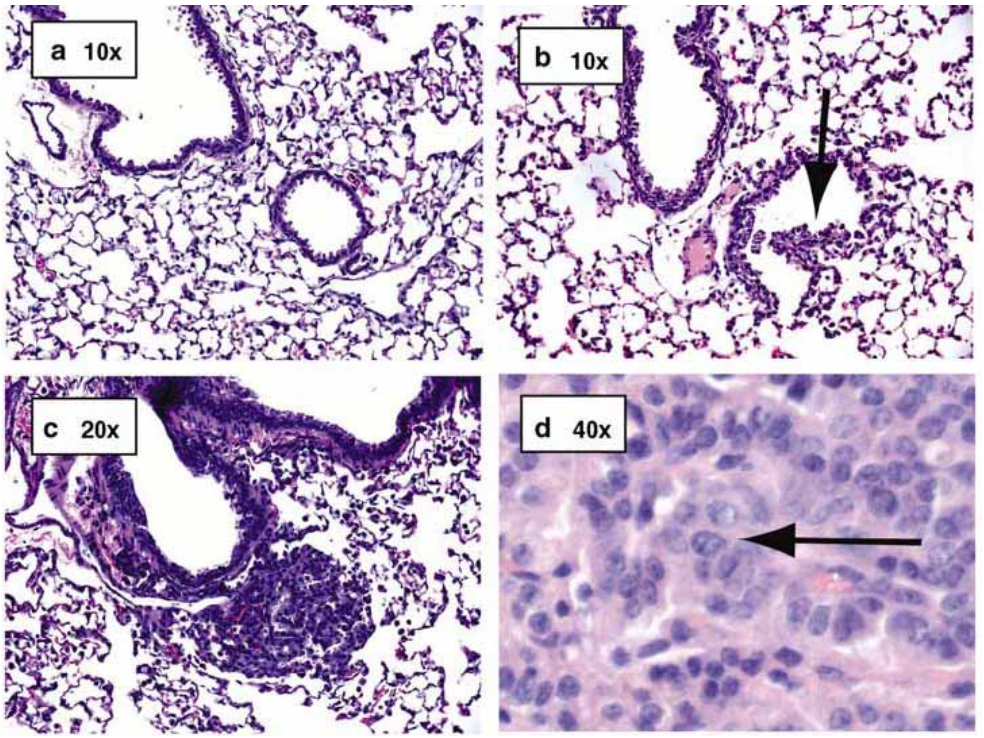
* G12D exon 2

Ji H, Oncogene. 2006

Modèle CC10-Cre/LSL-K-ras

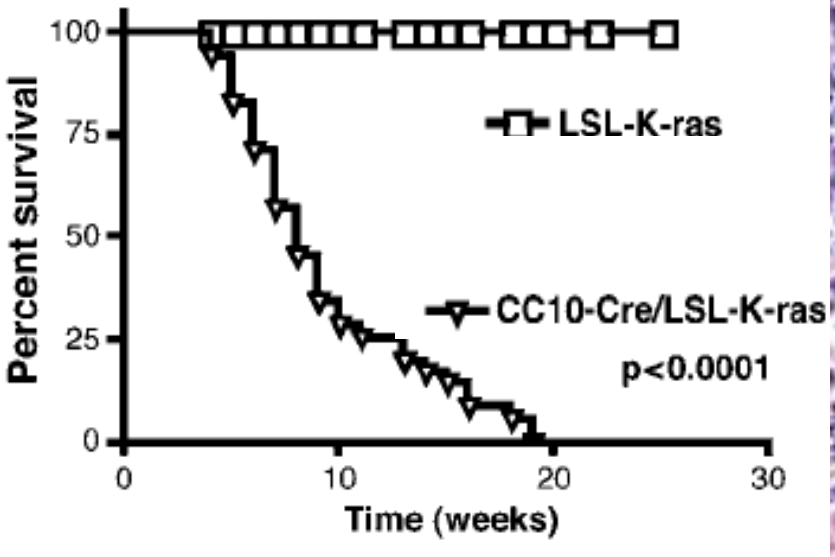
inflammation alvéolaire

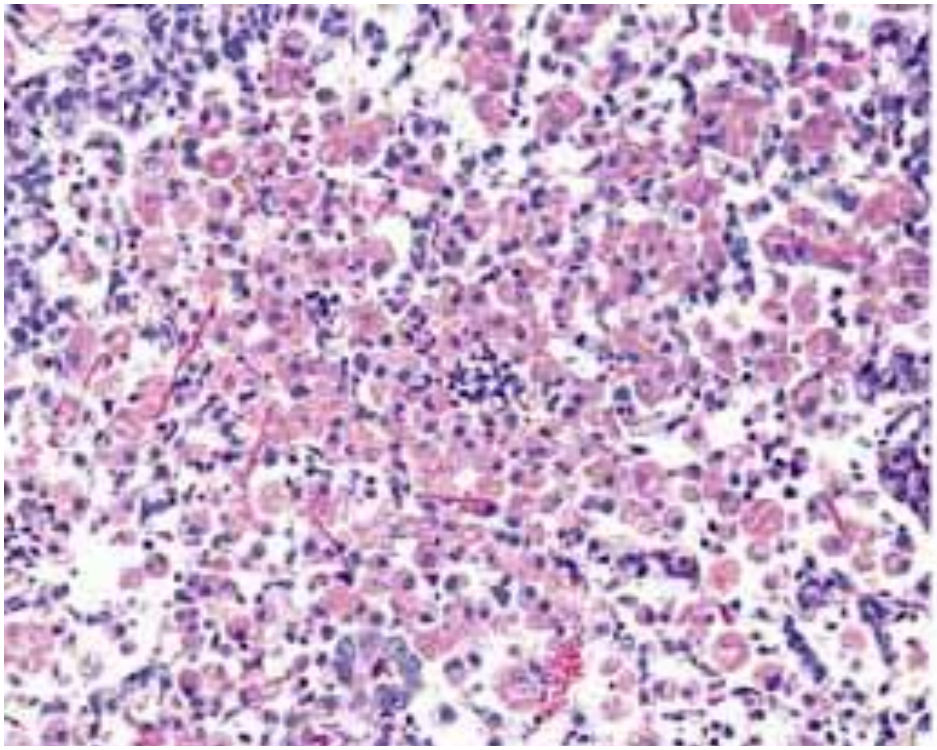




Ji H, Oncogene. 2006;65:2105-2112

Modèle CC10-Cre/LSL-K-ras
inflammation alvéolaire

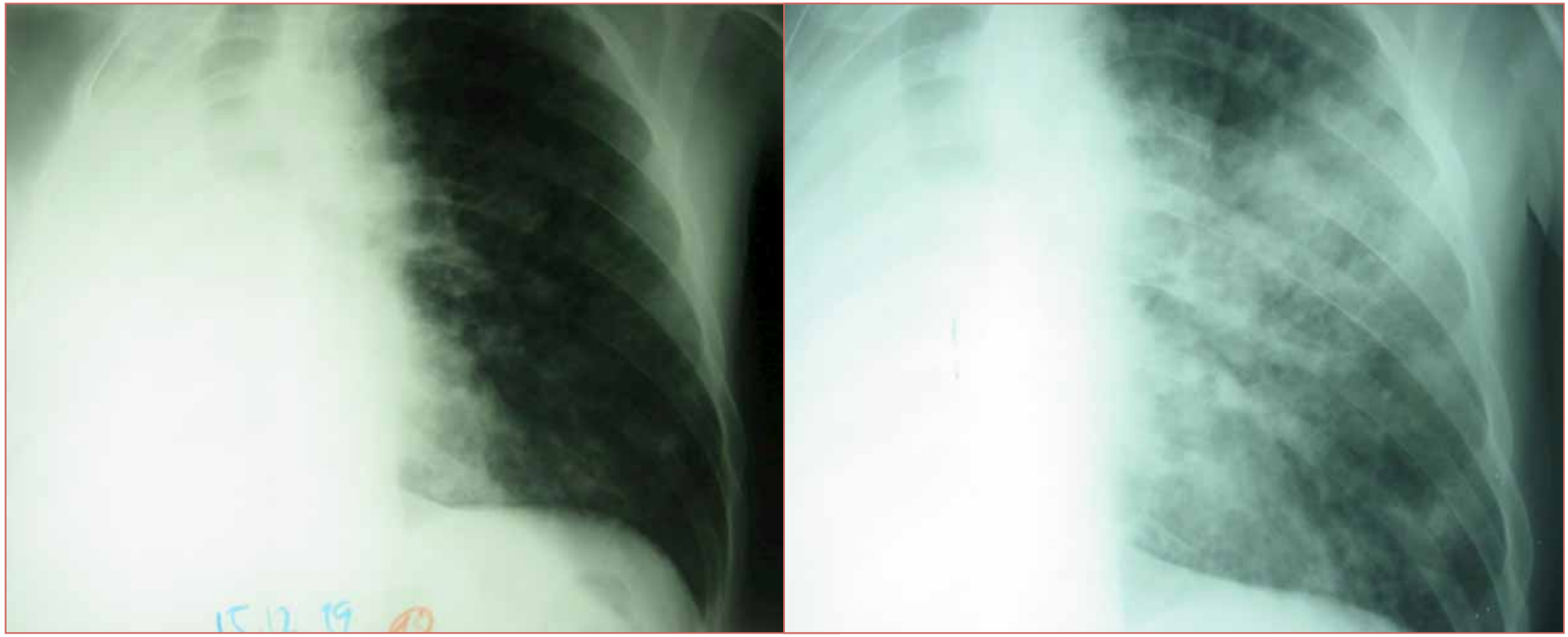




Ji H, Oncogene. 2006

Inflammation et cancer :

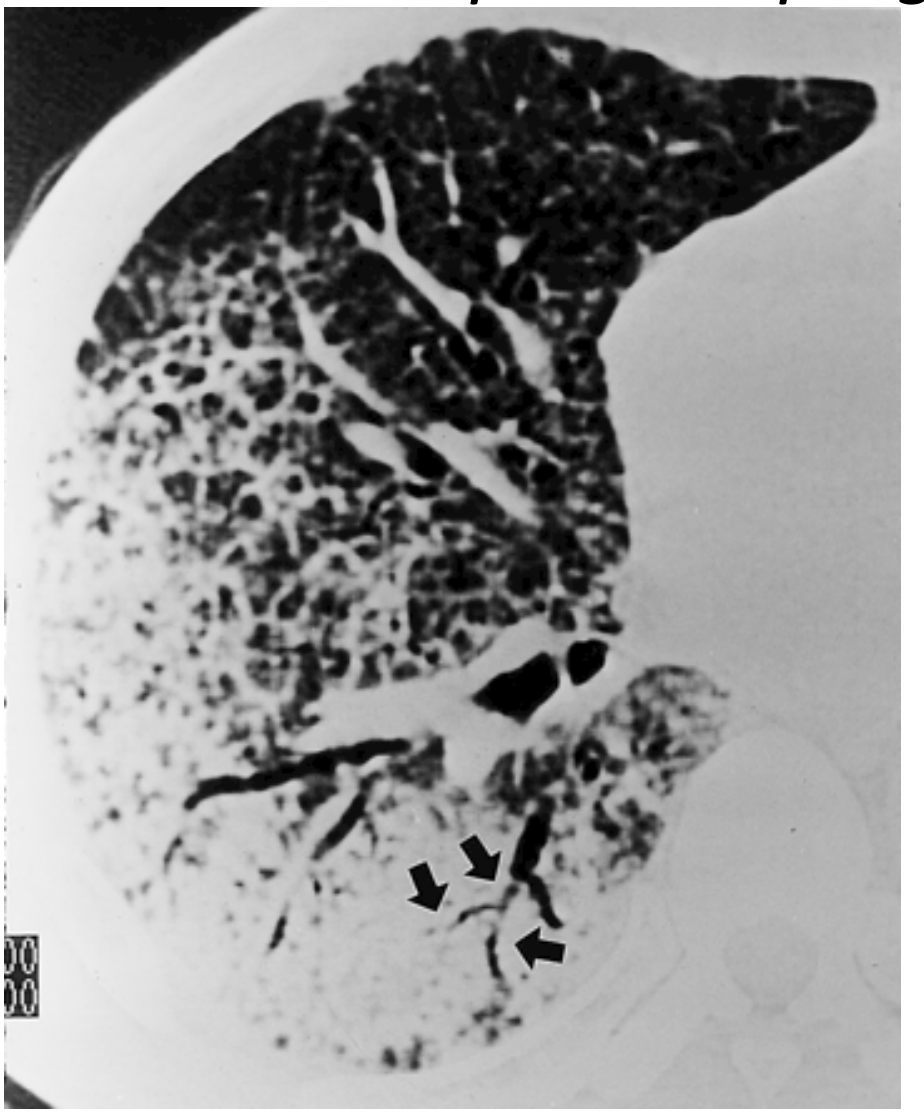
neutrophiles et progression aérogène



Wislez M, Chest. 2003

Inflammation et cancer :

neutrophiles et progression aérogène



Bronchorrhée
Crépitants
Lésions multilobaires
Inflammation alvéolaire

Wislez M, Chest. 2003

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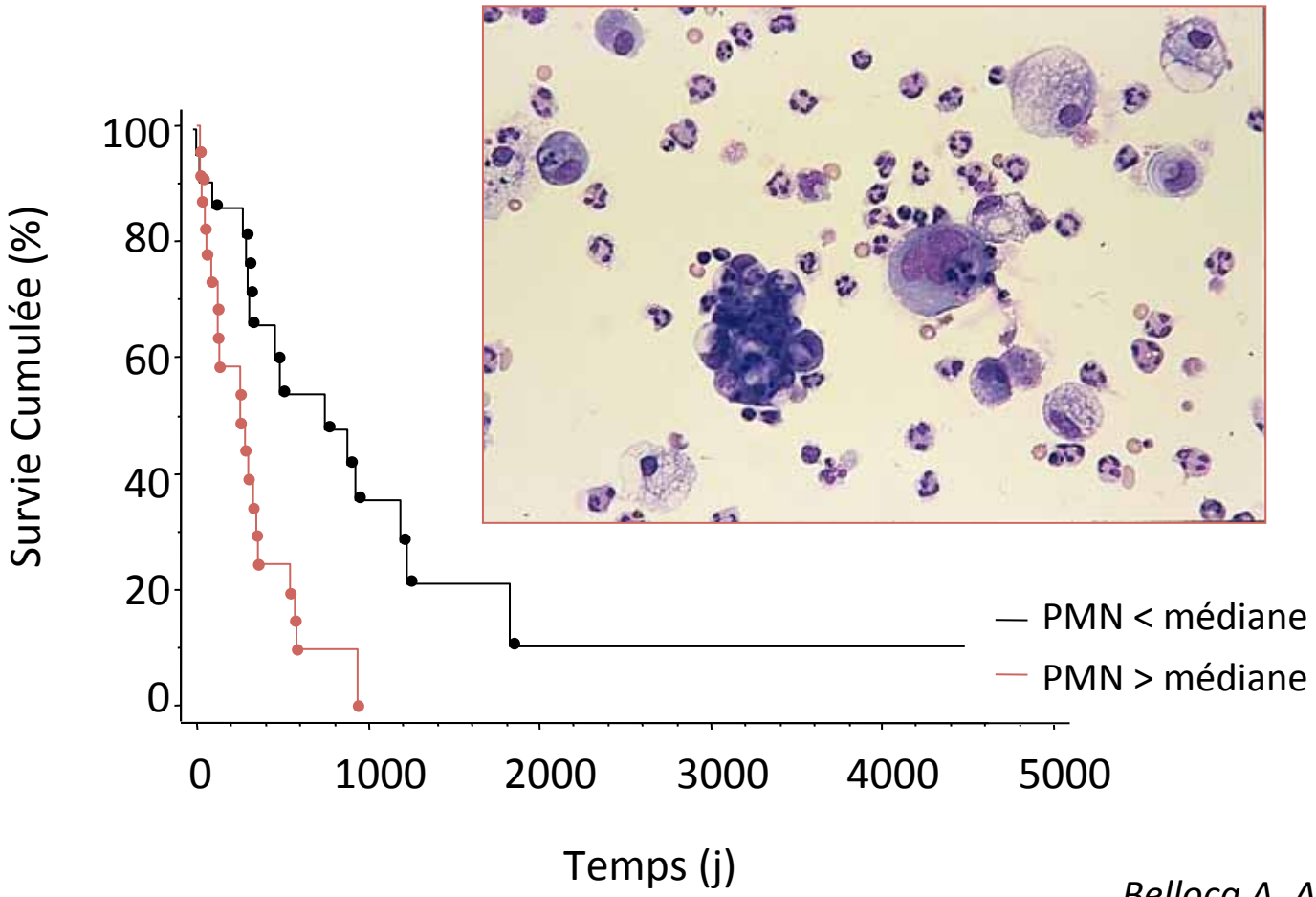

Bellocq A, Am J Pathol.1998

Inflammation et cancer :

mécanismes

Inflammation et cancer :

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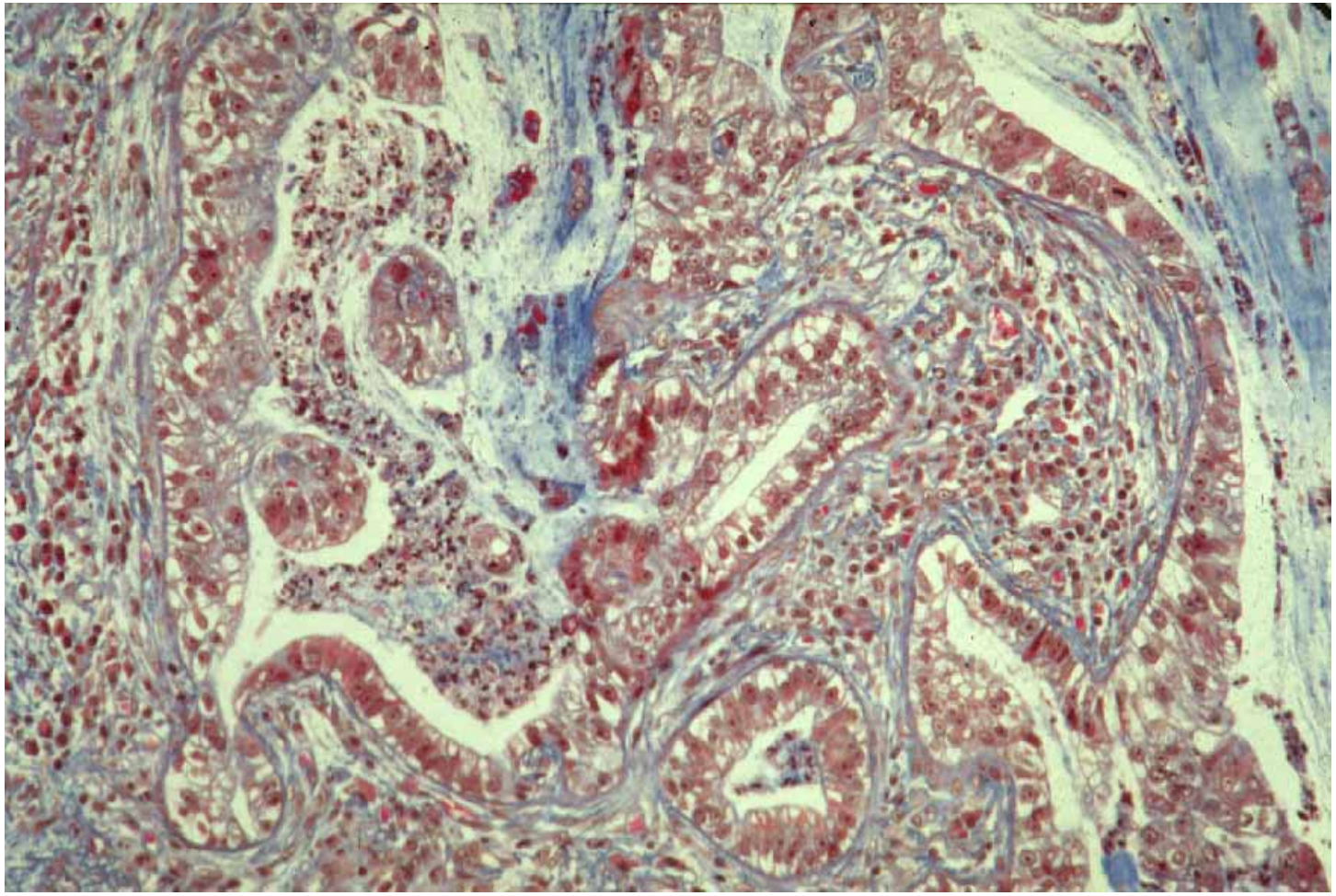
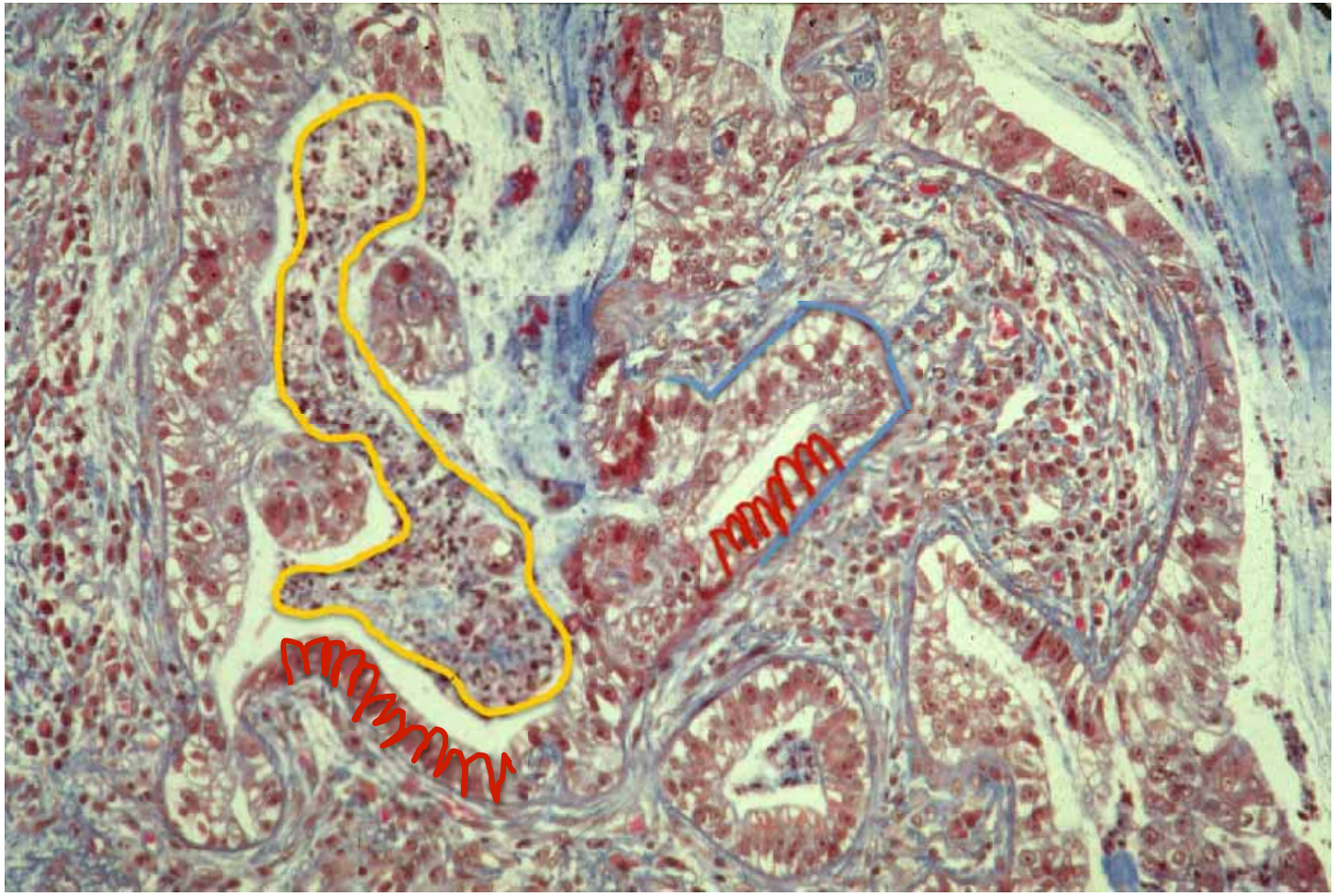


Inflammation et cancer :

neutrophiles et progression aérogène



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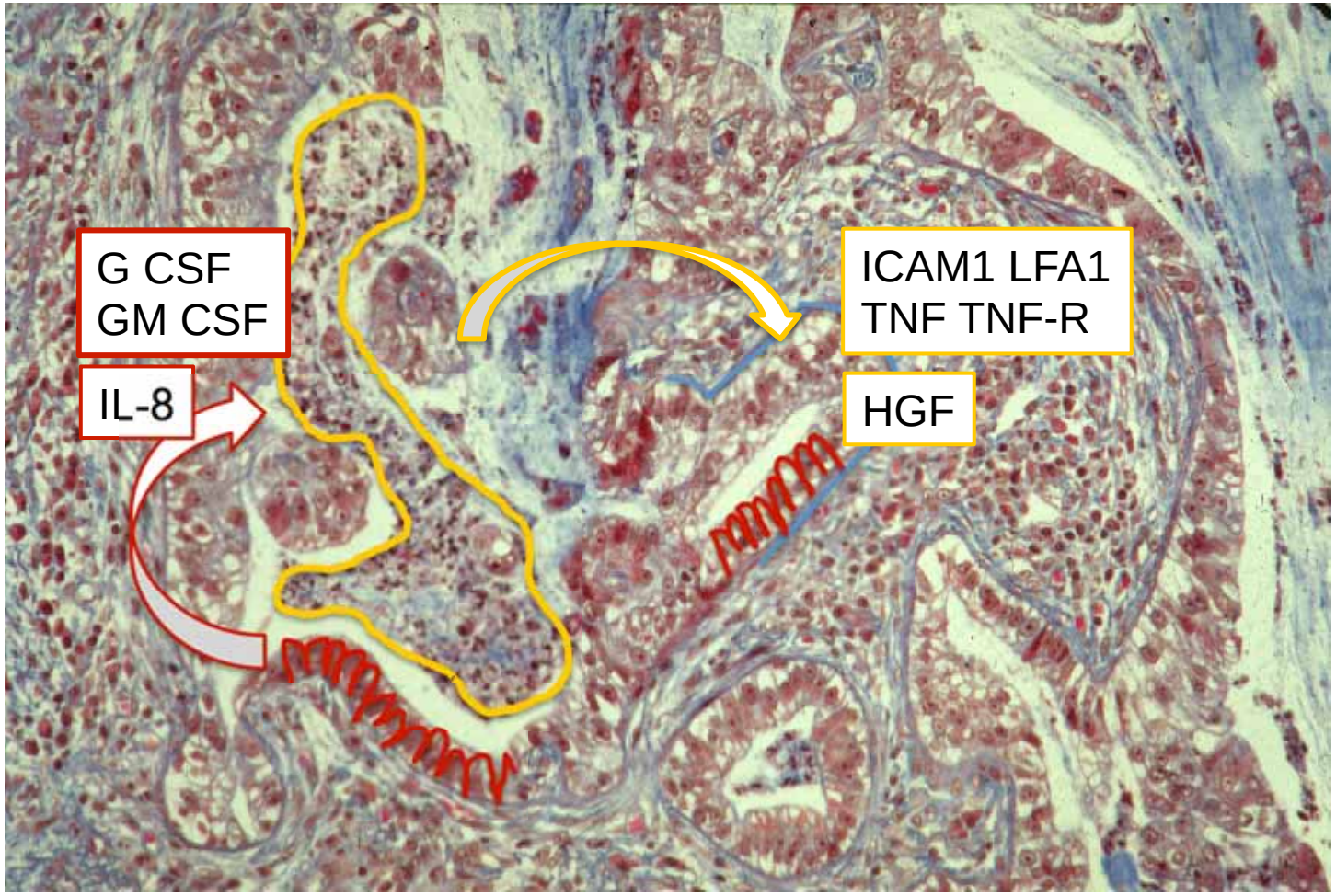
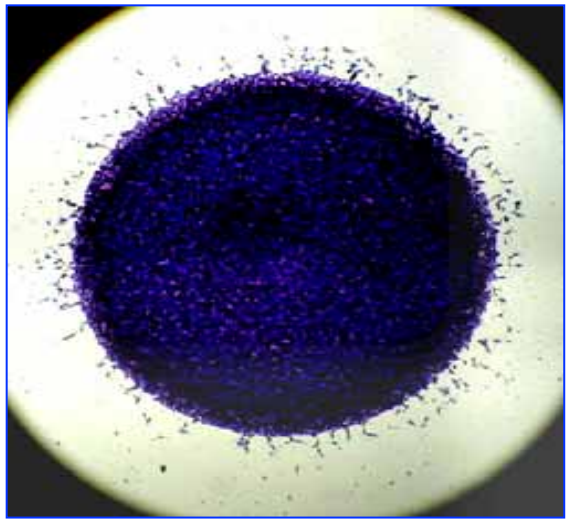


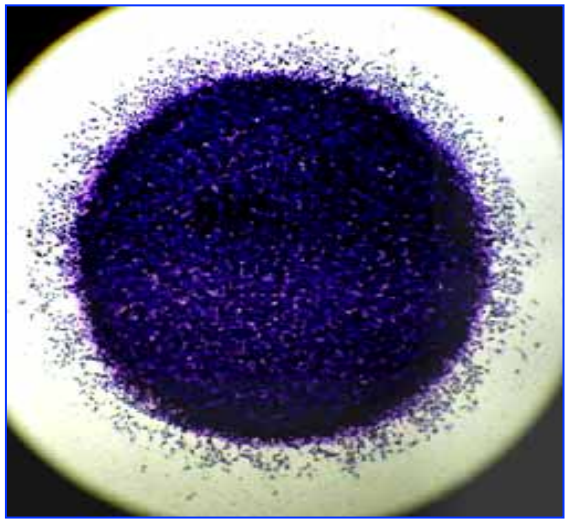
Neutrophiles et cancer :

HGF et progression aérogène

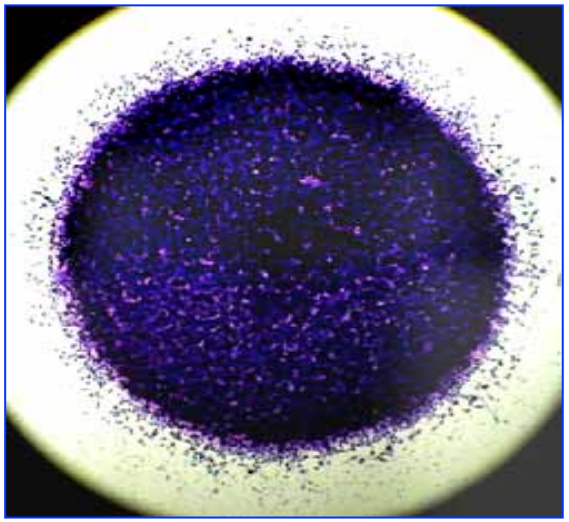
- Motilité cellulaire tumorale



LBA contrôle



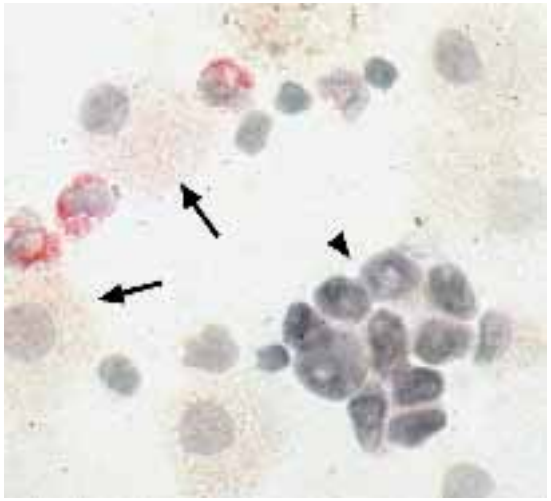
LBA ADC



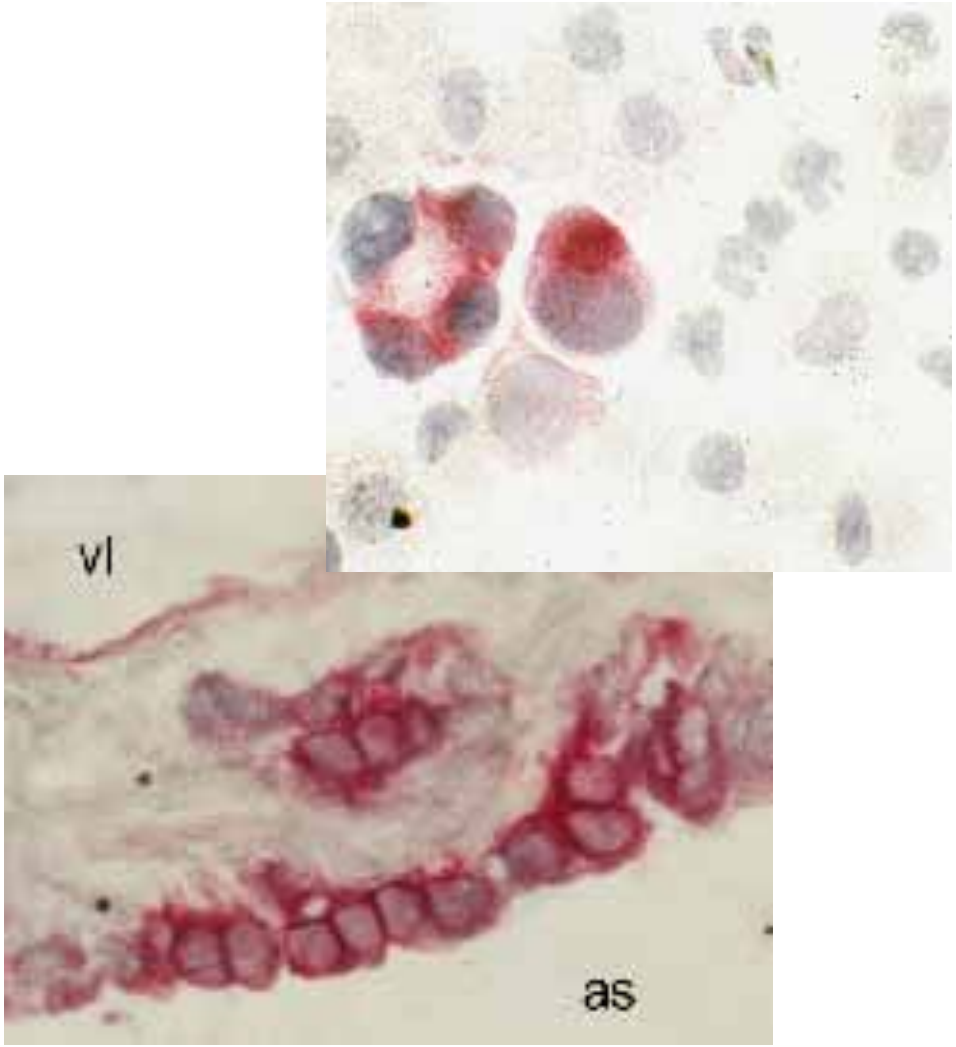
LBA ADC +
Ac. Anti-HGF

Wislez M, Cancer Res. 2003

HGF



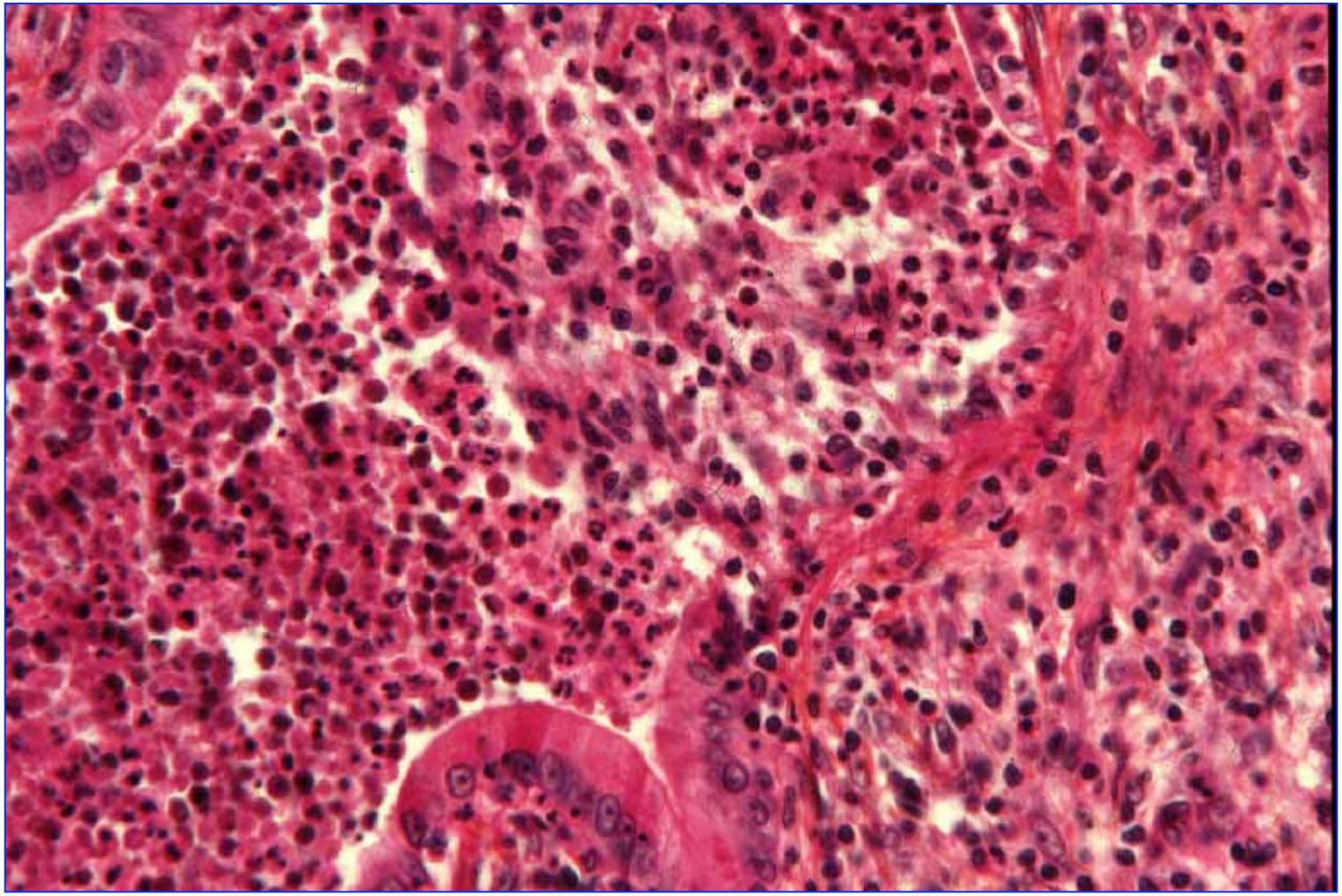
c-Met



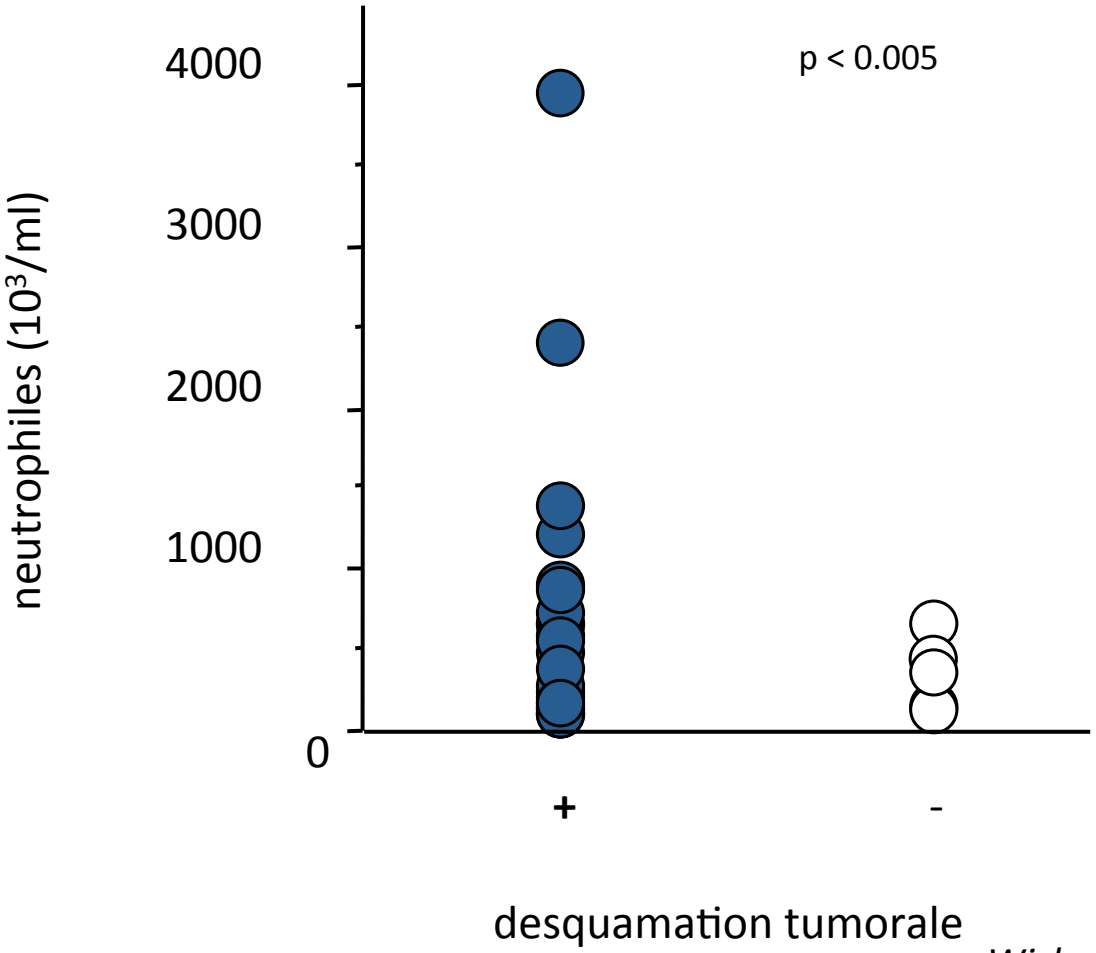
Wislez M, Cancer Res. 2003

Inflammation et cancer :

neutrophiles et progression aérogène



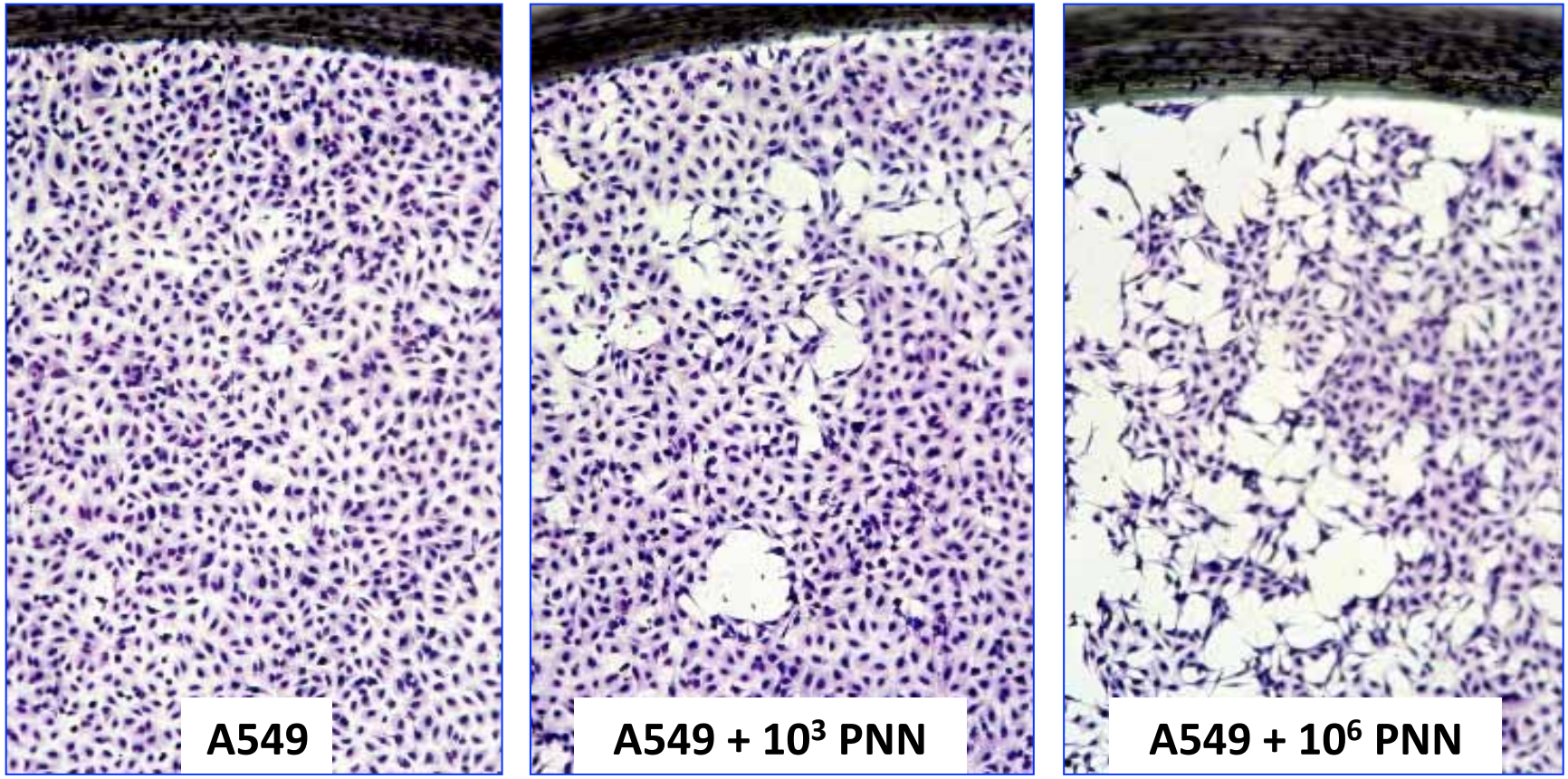
Neutrophiles et cancer :
desquamation tumorale



Wislez M, Clin Cancer Res. 2007

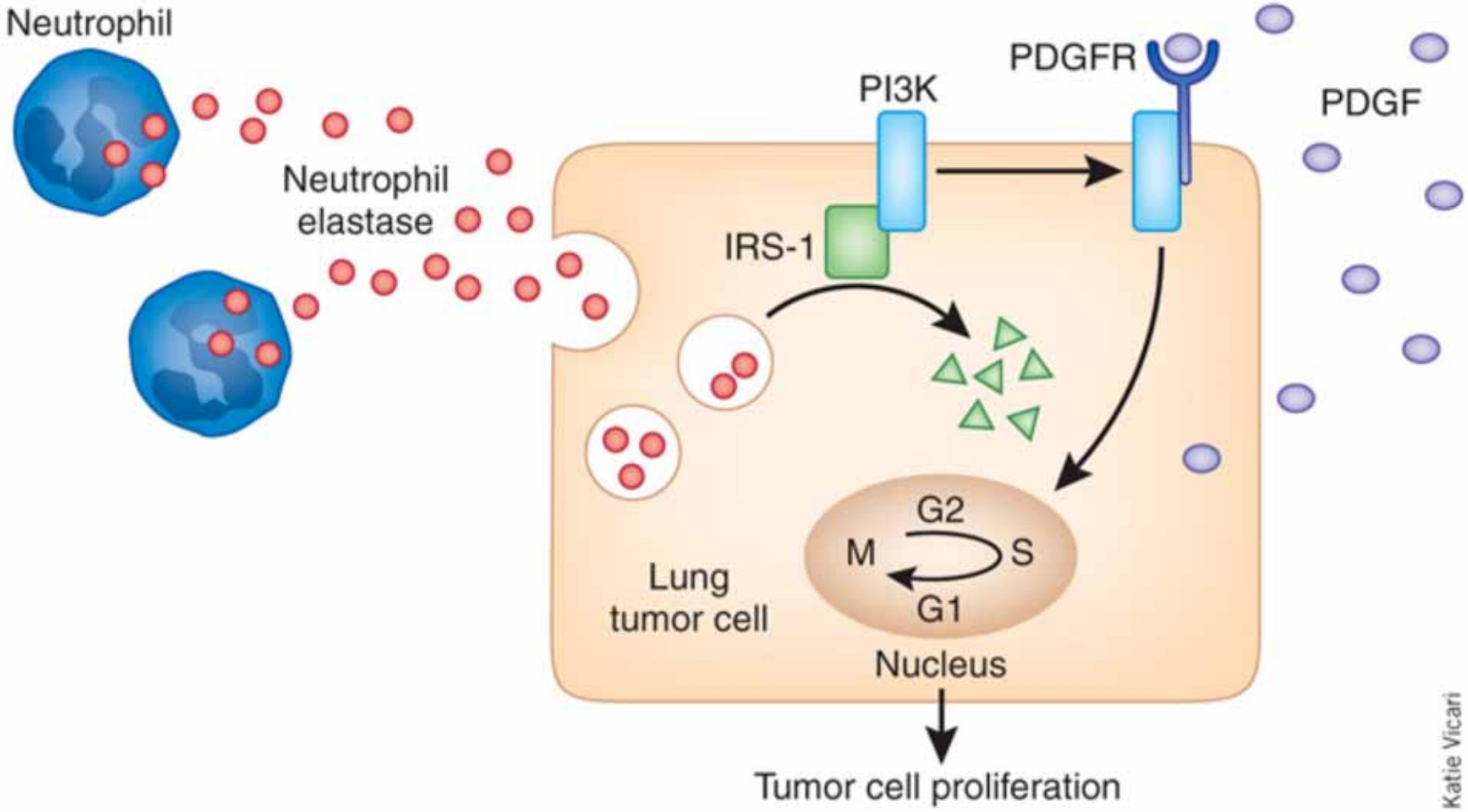
Neutrophiles et cancer :
desquamation tumorale

- phénomène de contact: rôle de TNF/TNF-R et ICAM1/LFA1



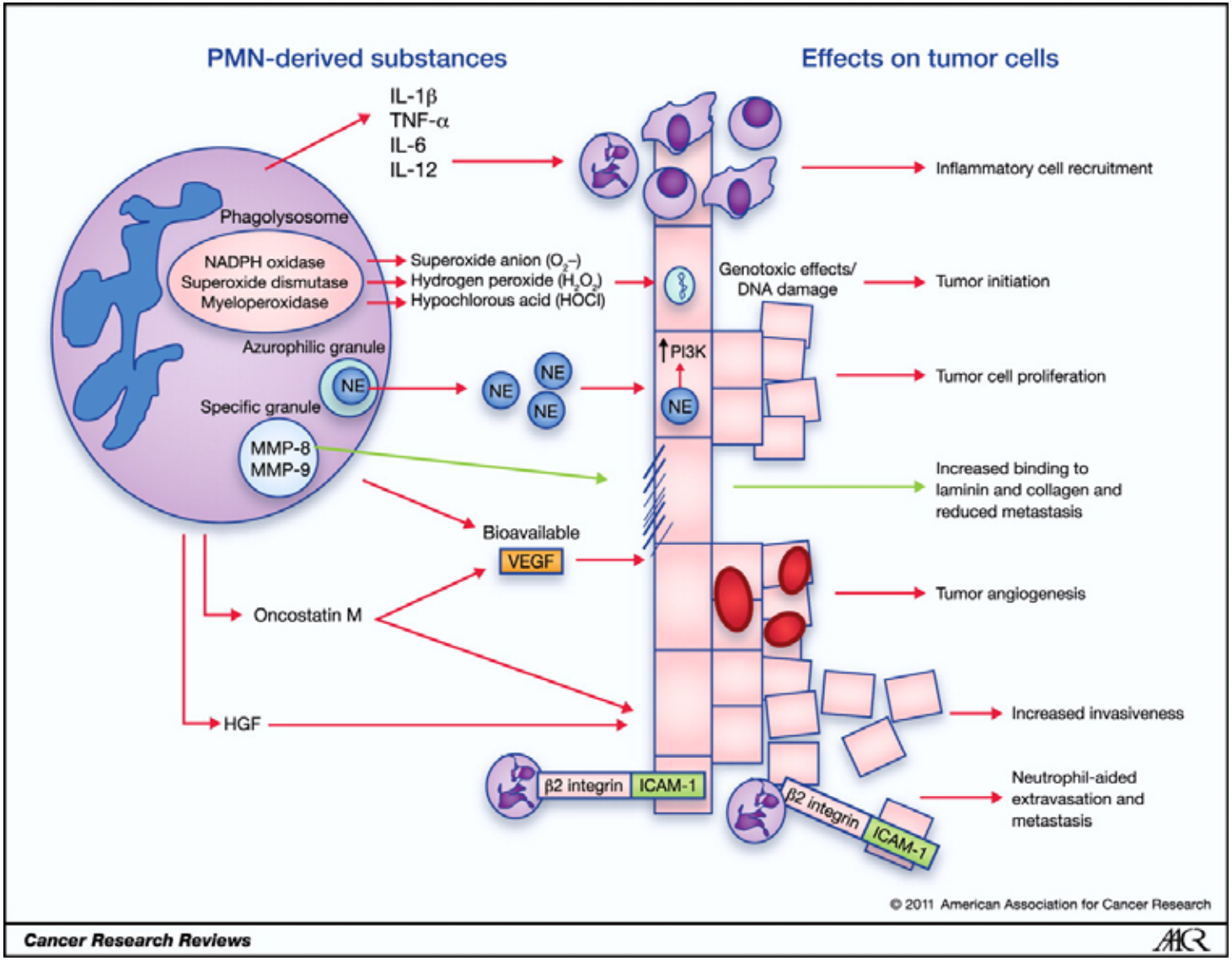
Wislez M, Clin Cancer Res. 2007

Neutrophiles et cancer :
rôle de l'élastase



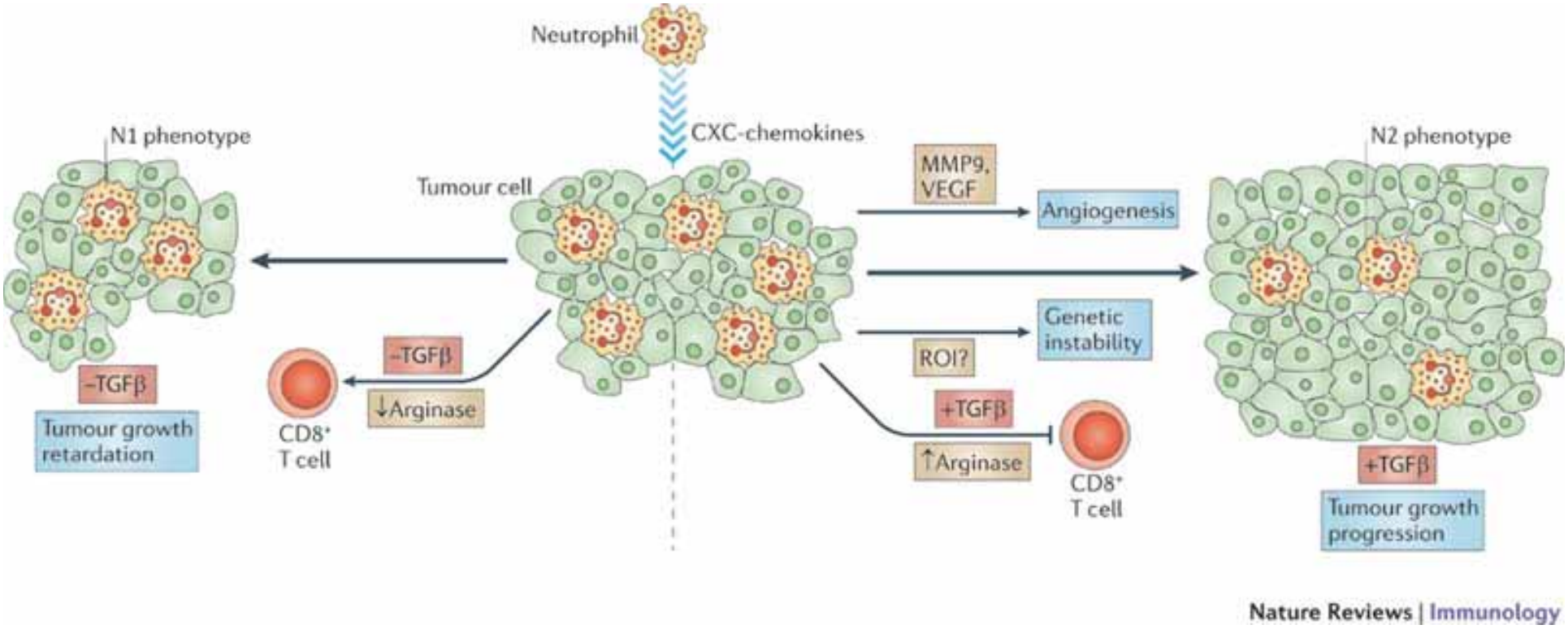
Houghton AM, Nat Med 2010

Neutrophiles et cancer



Alyssa D. Gregory, Cancer Res 2011

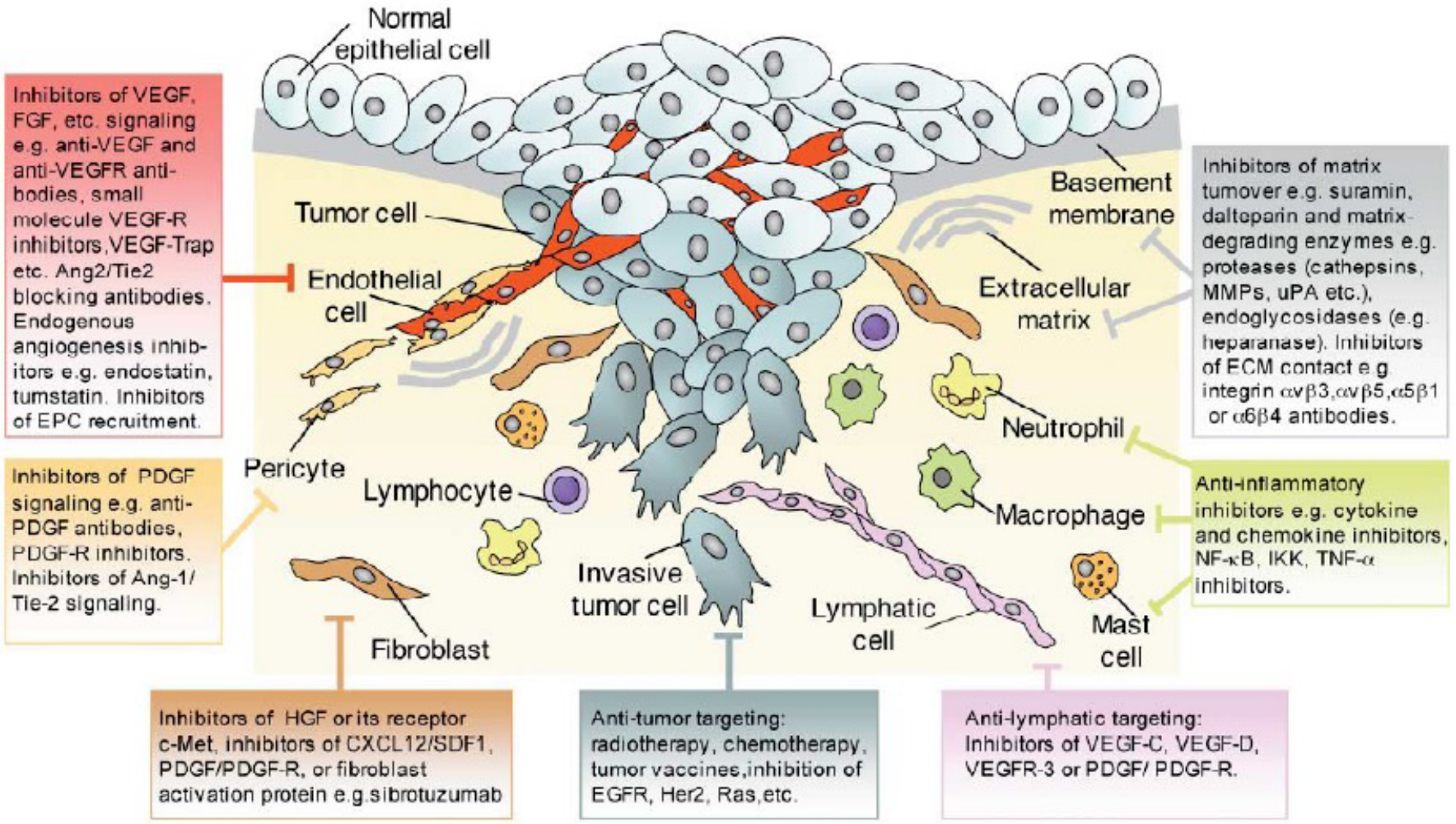
Neutrophiles et cancer :
dualité



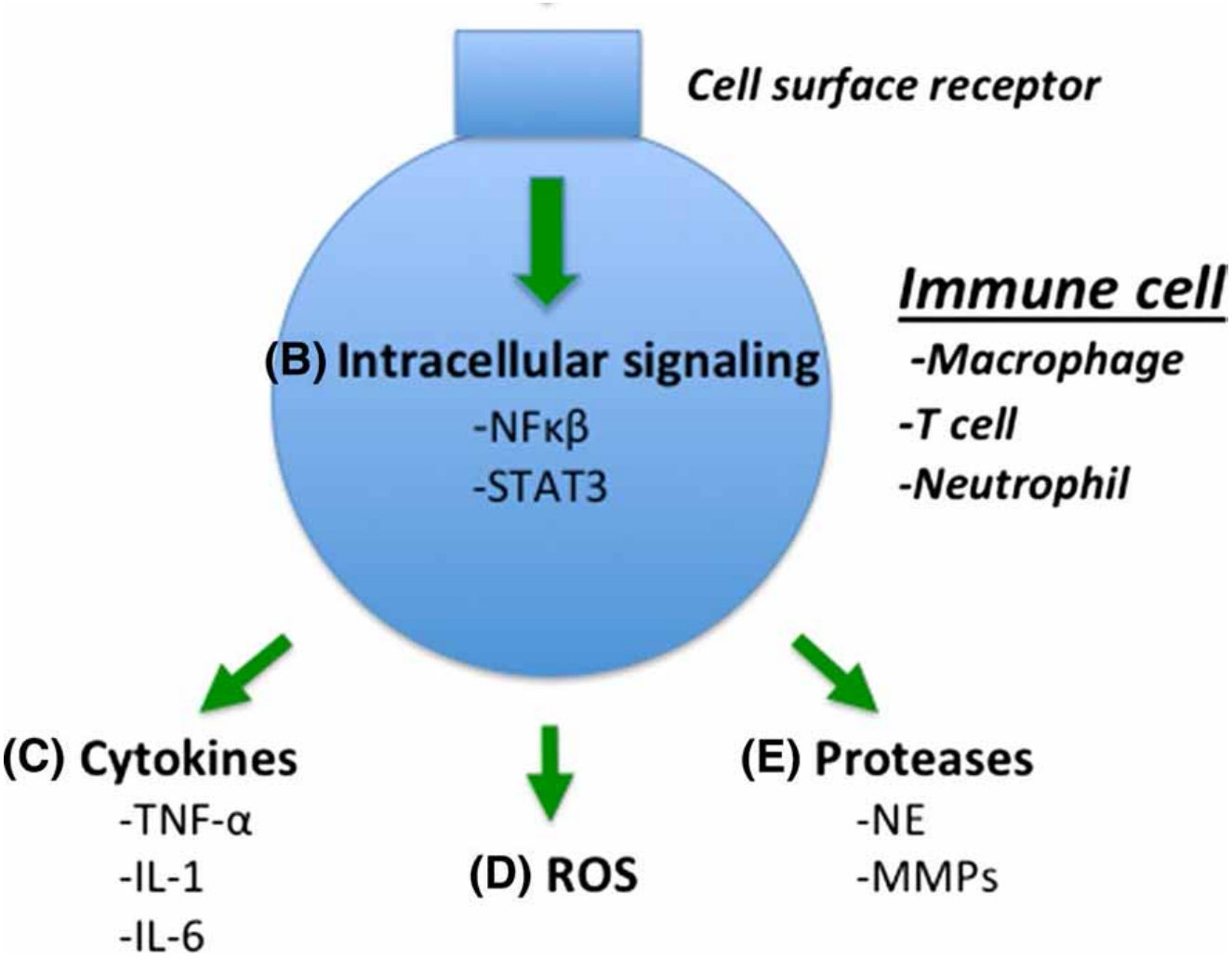
Fridlender ZG, Cancer Cell 2009

Inflammation et cancer

complexité des mécanismes



Inflammation et cancer :
quelles cibles thérapeutiques?



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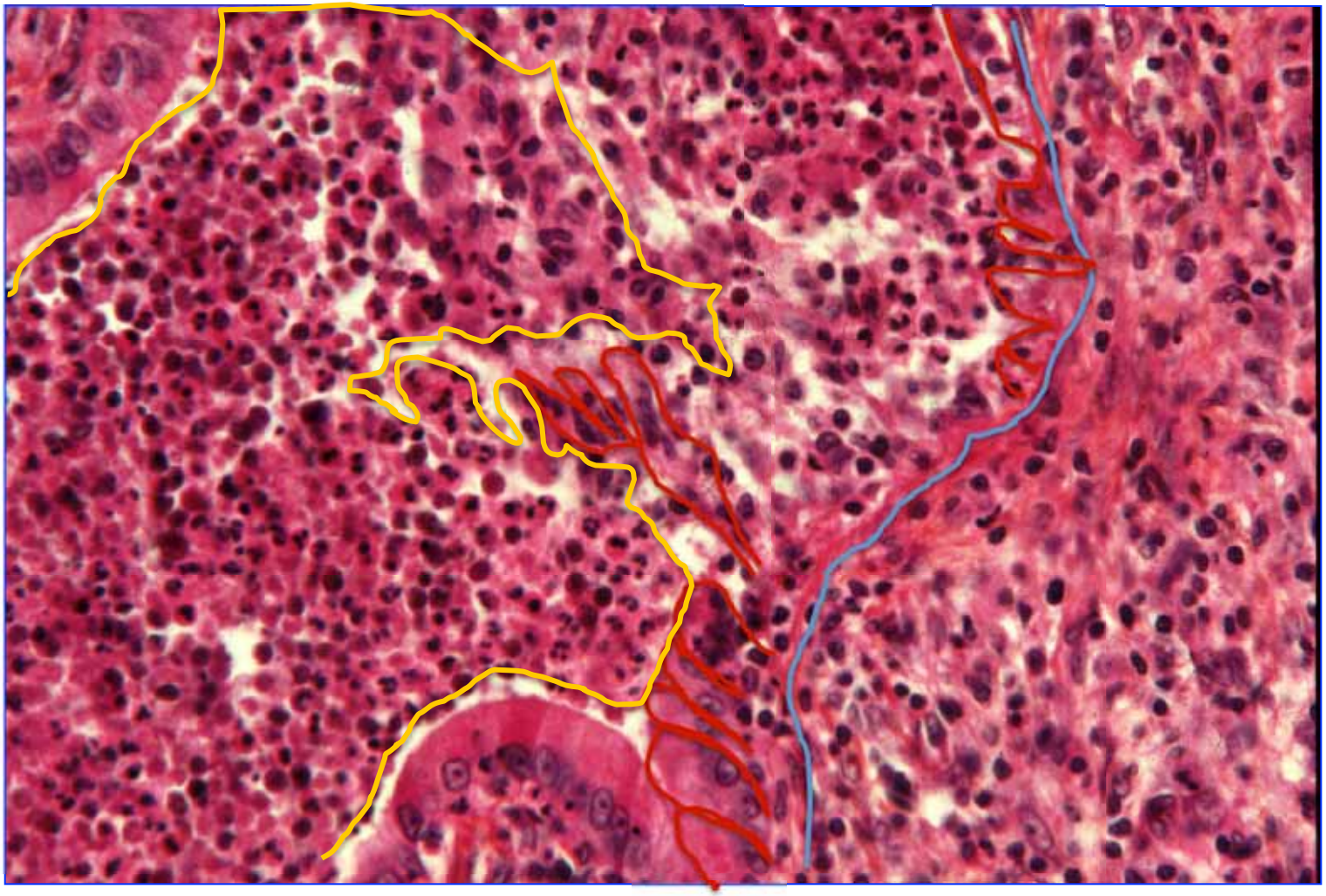
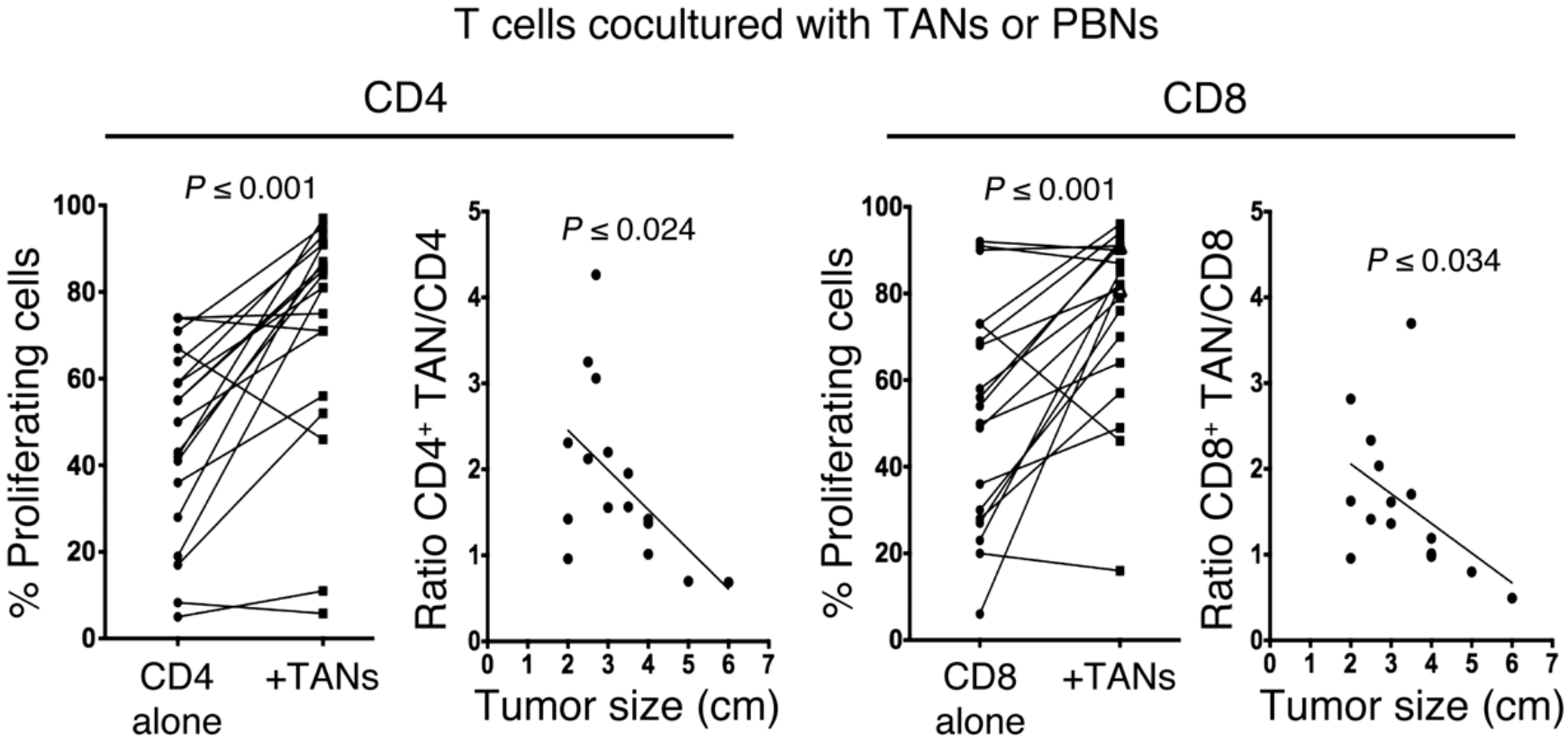
neutrophiles et progression aérogène



Neutrophiles et cancer : *dualité*



Erslanov E, J Clin Invest 2014

Cross talk immunité et inflammation