

Biologie et Facteurs Pronostiques du Myélome Multiple

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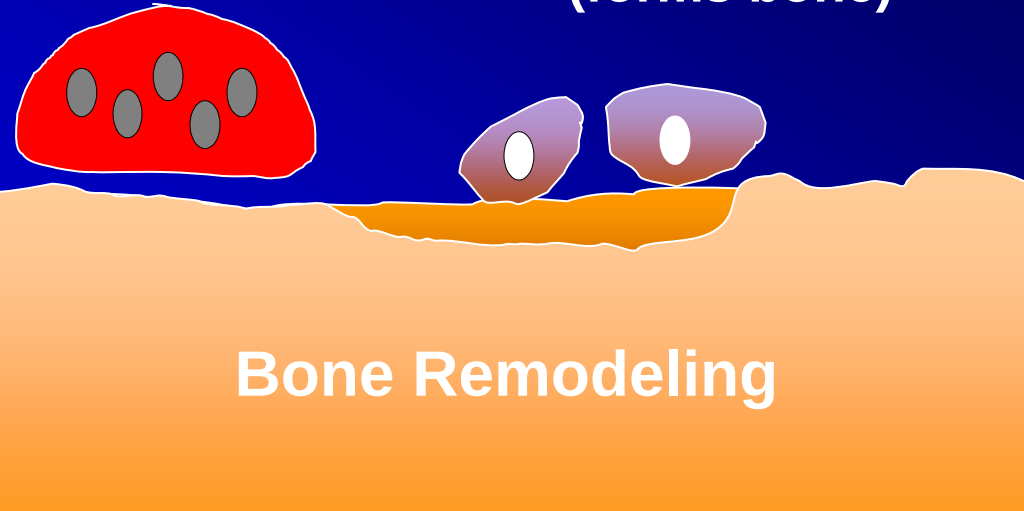
**Systeme rank-rank ligand :
importance dans la
physiopathologie du myélome et
intérêt thérapeutique**

Normal Bone

Remodeling/Bone Mass is Maintained Via the Balance of Bone Formation and Bone Resorption

**Osteoclast
(resorbs bone)**

**Osteoblast
(forms bone)**



Pathologic Bone

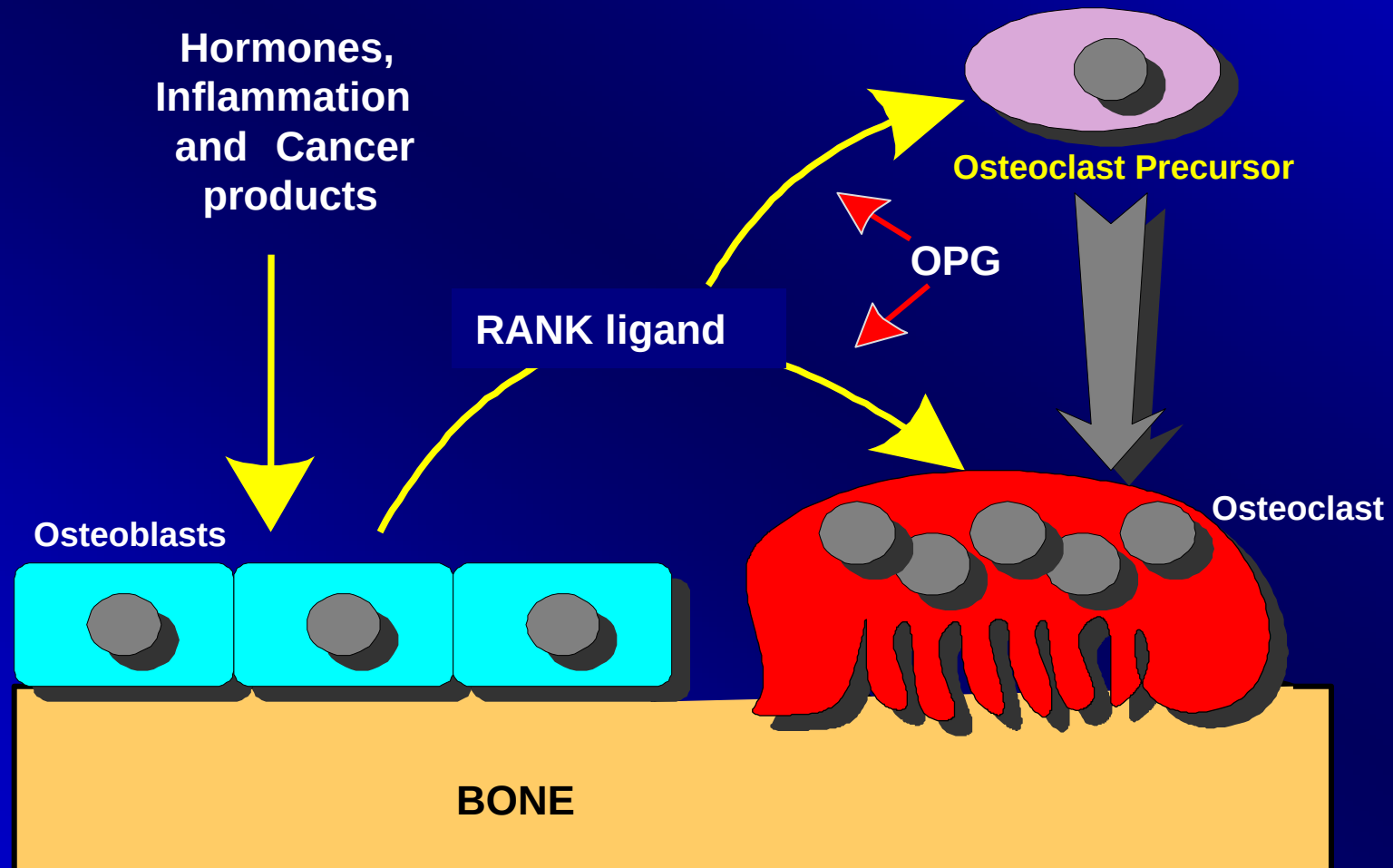
Resorption is Mediated by Excessive Osteoclast-Mediated Remodeling

- Osteoporosis
- Arthritic bone erosion
- Multiple myeloma
- Bone metastasis

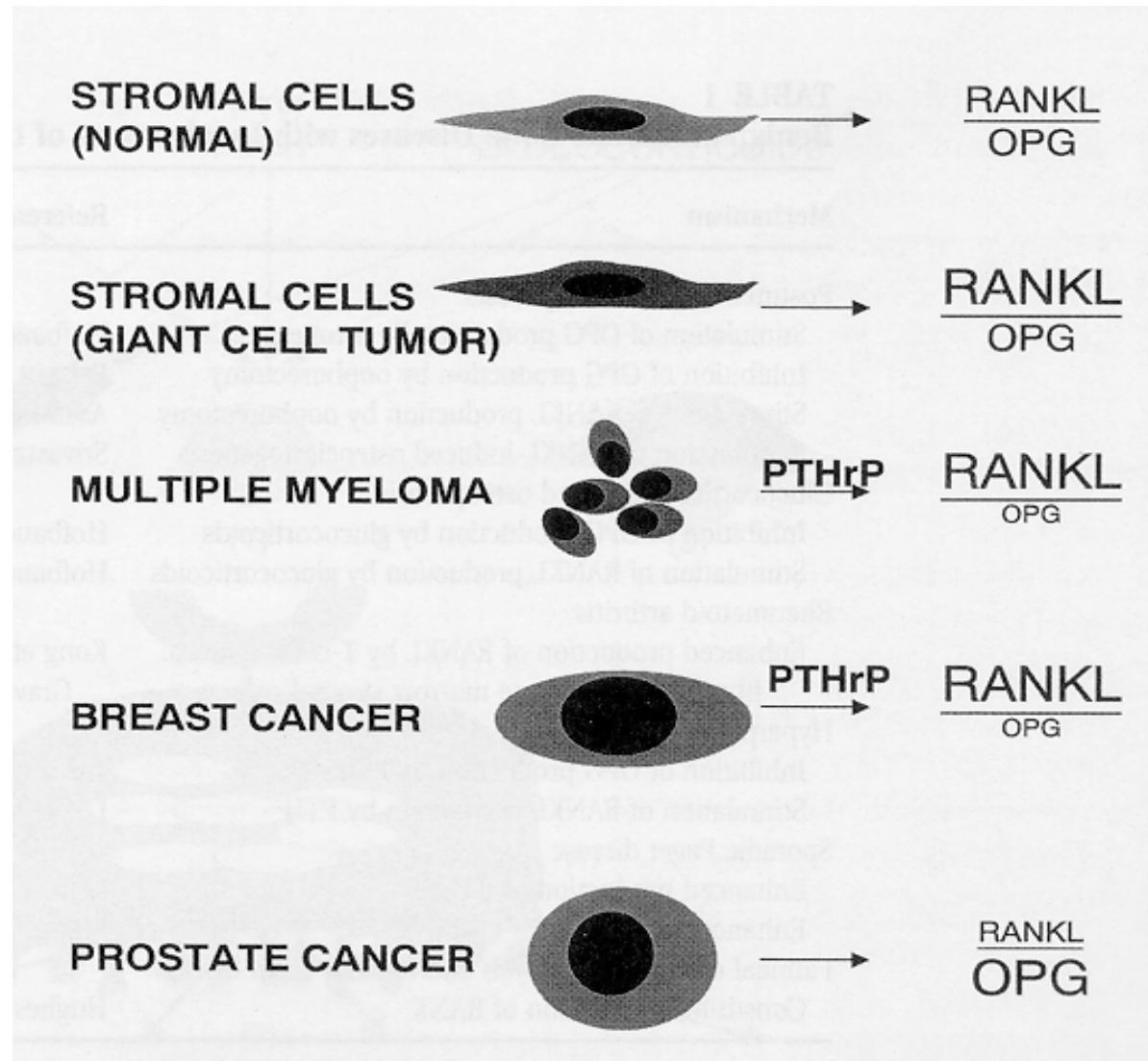


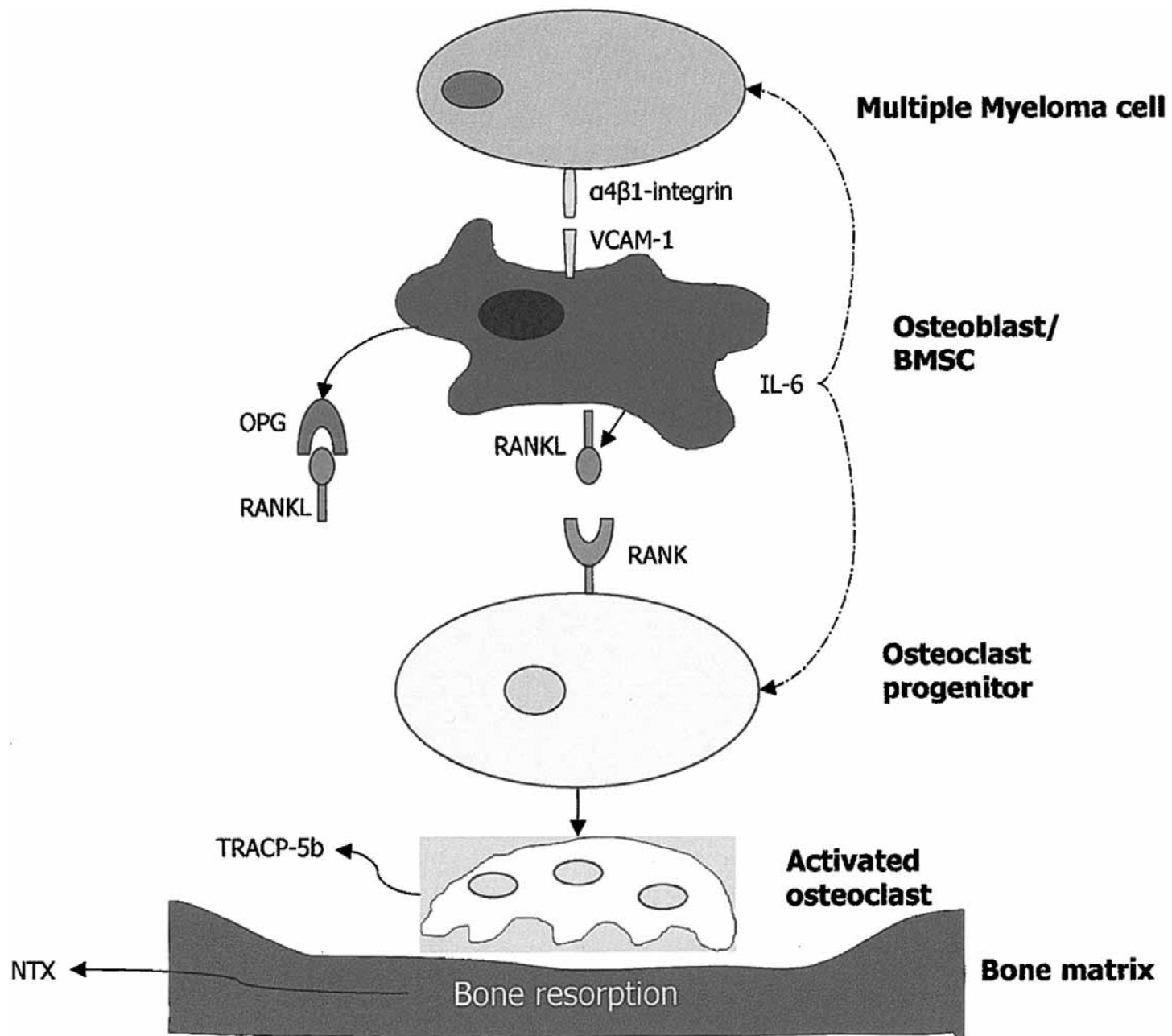
Cell Signaling in the Control of Bone Cell Function

- The RANK / RANK-L and OPG System



OPG / OPGL system in various malignancies





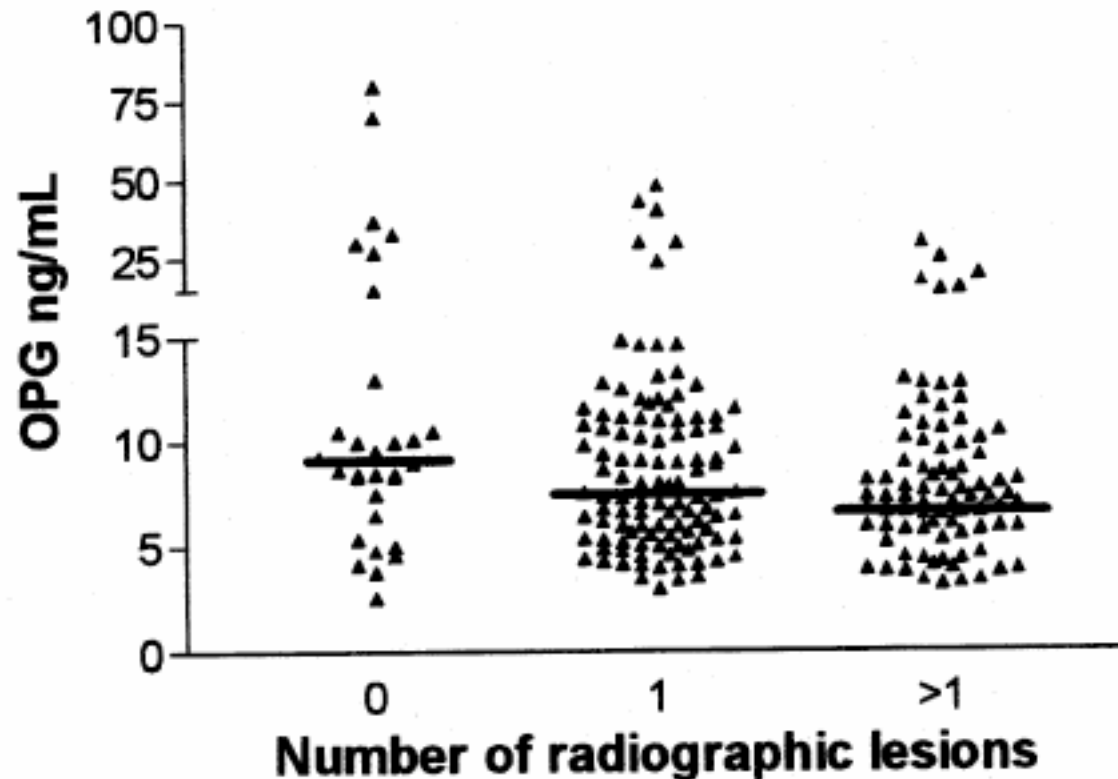
Terpos et al. Blood 2003; 102, 1064-1069

Bone resorption markers levels within different groups mean $\pm$ SD, median (number of patients)

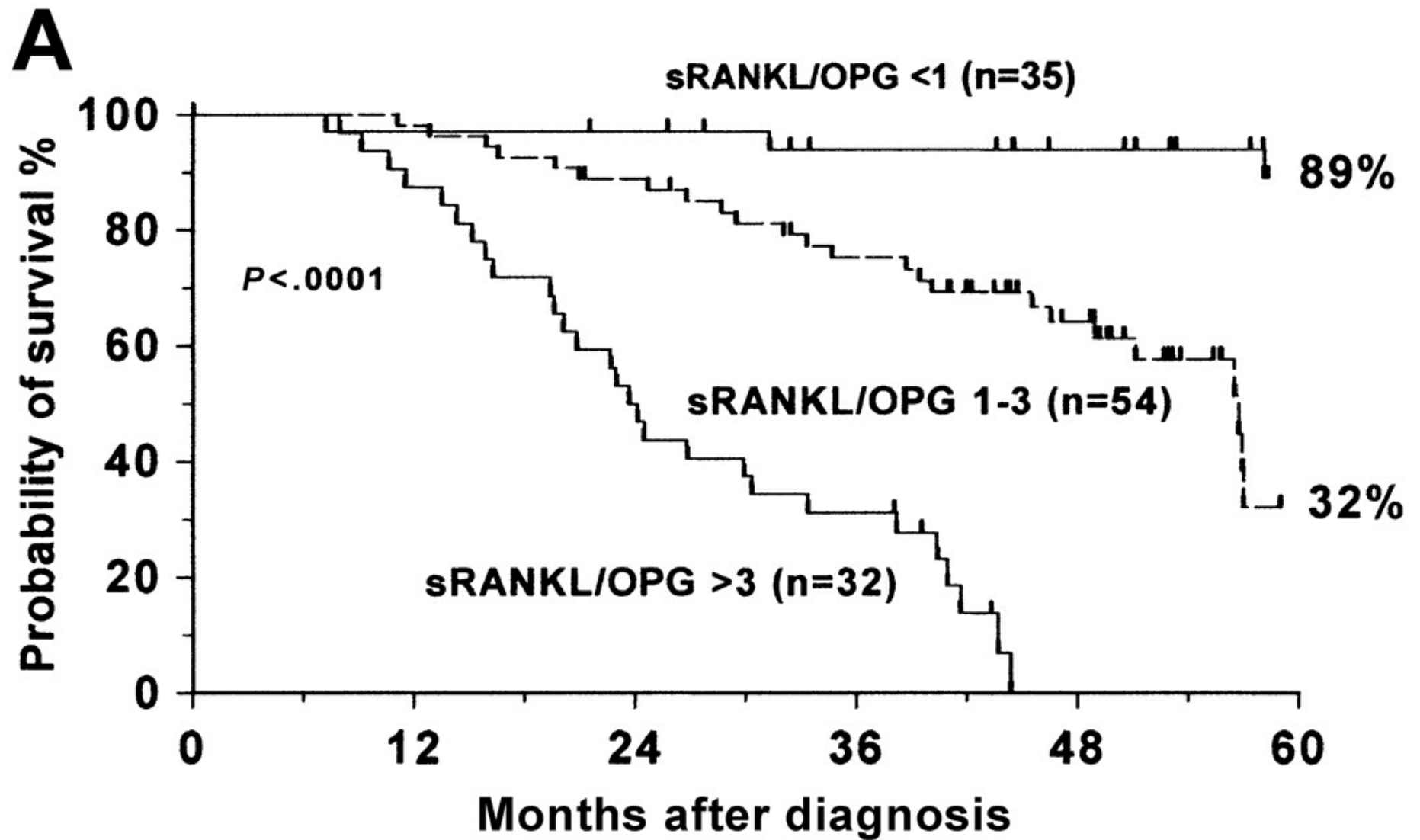
	MGUS	MM I	MM II/III	MM plateau	MM relapse
DPD	5.7 $\pm$ 2.6 4.9 (38)	5.6 $\pm$ 2.9 5.0 (45)	8.0 $\pm$ 4.3 6.8 (76)	6.9 $\pm$ 3.7 5.6 (48)	9.6 $\pm$ 5.7 8.4 (41)
CTX	161 $\pm$ 120 122 (32)	163 $\pm$ 125 130 (33)	408 $\pm$ 311 283 (61)	142 $\pm$ 148 110 (33)	317 $\pm$ 342 166 (30)
NTX	37 $\pm$ 27 31.4 (32)	51 $\pm$ 42 33.6 (33)	121 $\pm$ 94 89.1 (61)	41 $\pm$ 47 29.5 (33)	89 $\pm$ 92 50.4 (30)

Serum OPG levels in patients with Multiple myeloma

Seidel et al. Blood 2001 ; 98: 2269



Serum OPG levels in myeloma grouped by degree of skeletal involvement



[CANCER RESEARCH 63, 912-916, March 1, 2003]

Advances in Brief

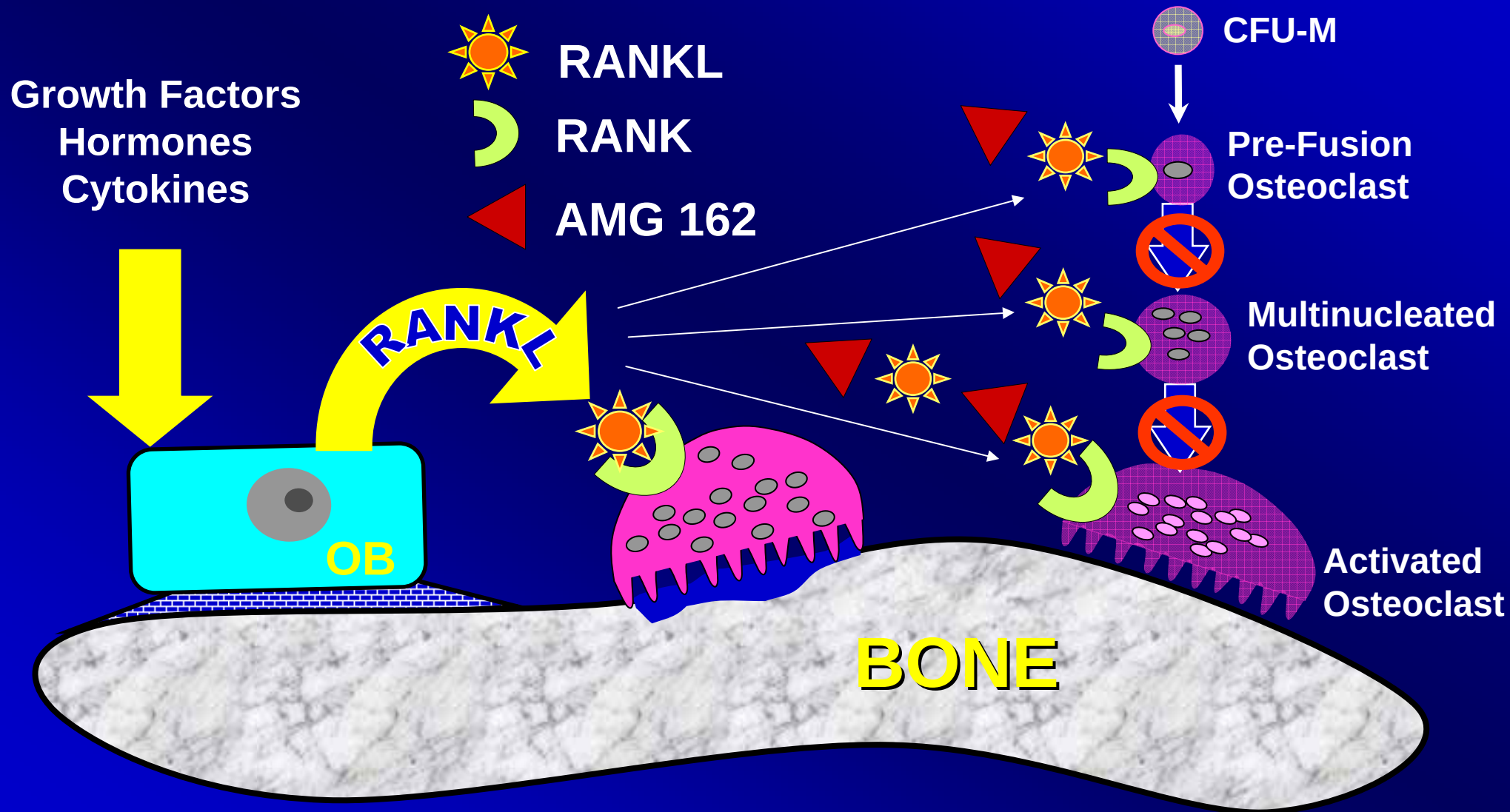
Osteoprotegerin Is a Soluble Decoy Receptor for Tumor Necrosis Factor-related Apoptosis-inducing Ligand/Apo2 Ligand and Can Function as a Paracrine Survival Factor for Human Myeloma Cells¹

Claire M. Shipman² and Peter I. Croucher

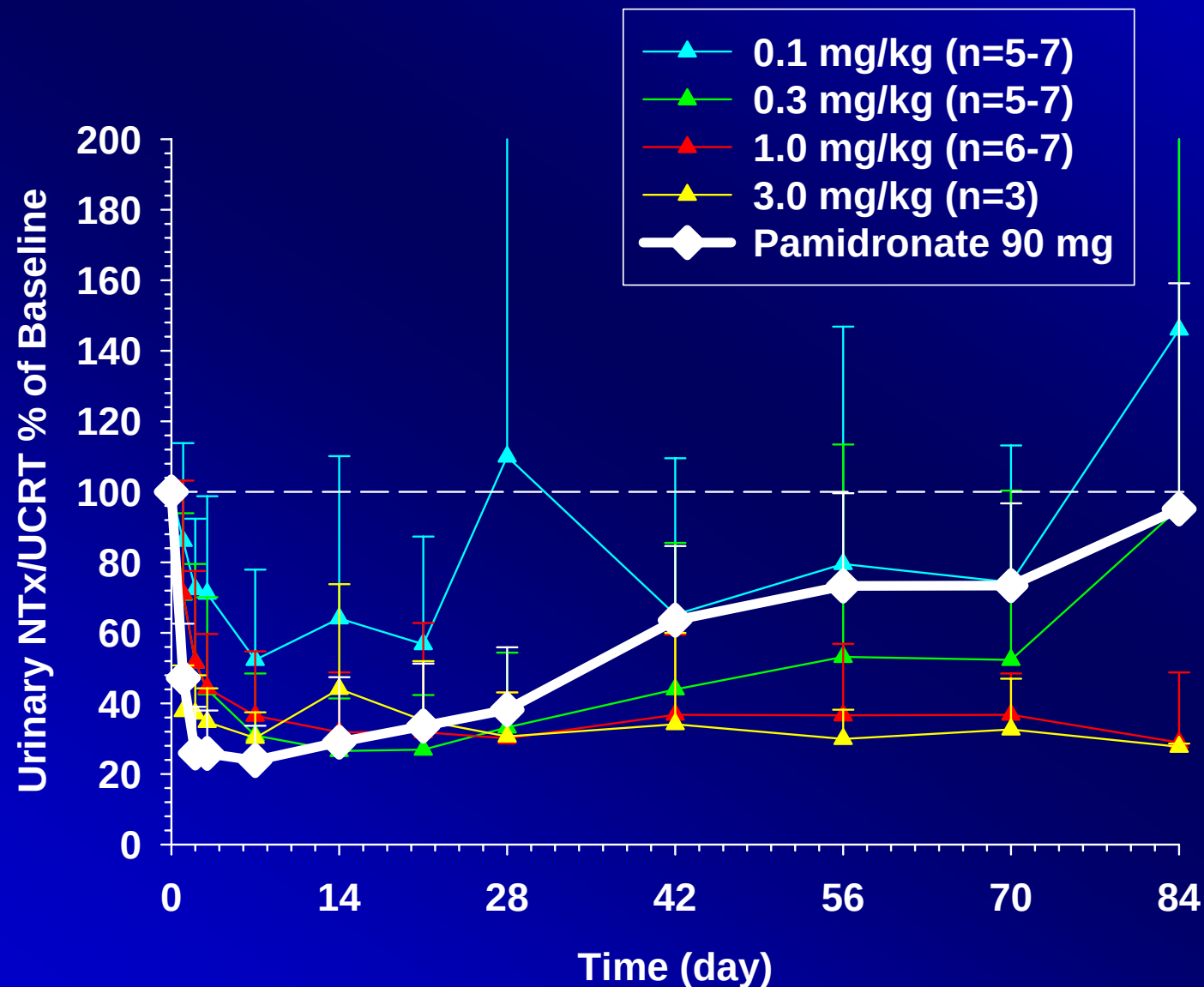
Nuffield Department of Orthopaedic Surgery, University of Oxford, Nuffield Orthopaedic Center, Oxford OX3 7LD, United Kingdom

RANK/RANKL Pathway

Mechanism of action of AMG 162



Inhibition de la résorption osseuse par l'anticorps anti-RANKL AMG162 (cancer du sein)



Facteurs Pronostiques du Myélome Multiple

Principaux facteurs de mauvais pronostic

Lié à l'hôte

Age élevé

Liés à la tumeur

- Masse tumorale

β 2microglobuline sérique élevée

- . Hémoglobine basse*
- . Calcémie élevée*
- . Lésions osseuses étendues*
- . Plasmocytose médullaire élevée

- Malignité intrinsèque

Anomalies chromosomiques**

-13/13q-, t(4;14), nb. chromosomes < 46

- . CRP élevée
- . Albumine sérique basse
- . LDH élevée
- Cinétique élevée**
- Caractéristiques des cellules MM**

Traitement

Chimiorésistance

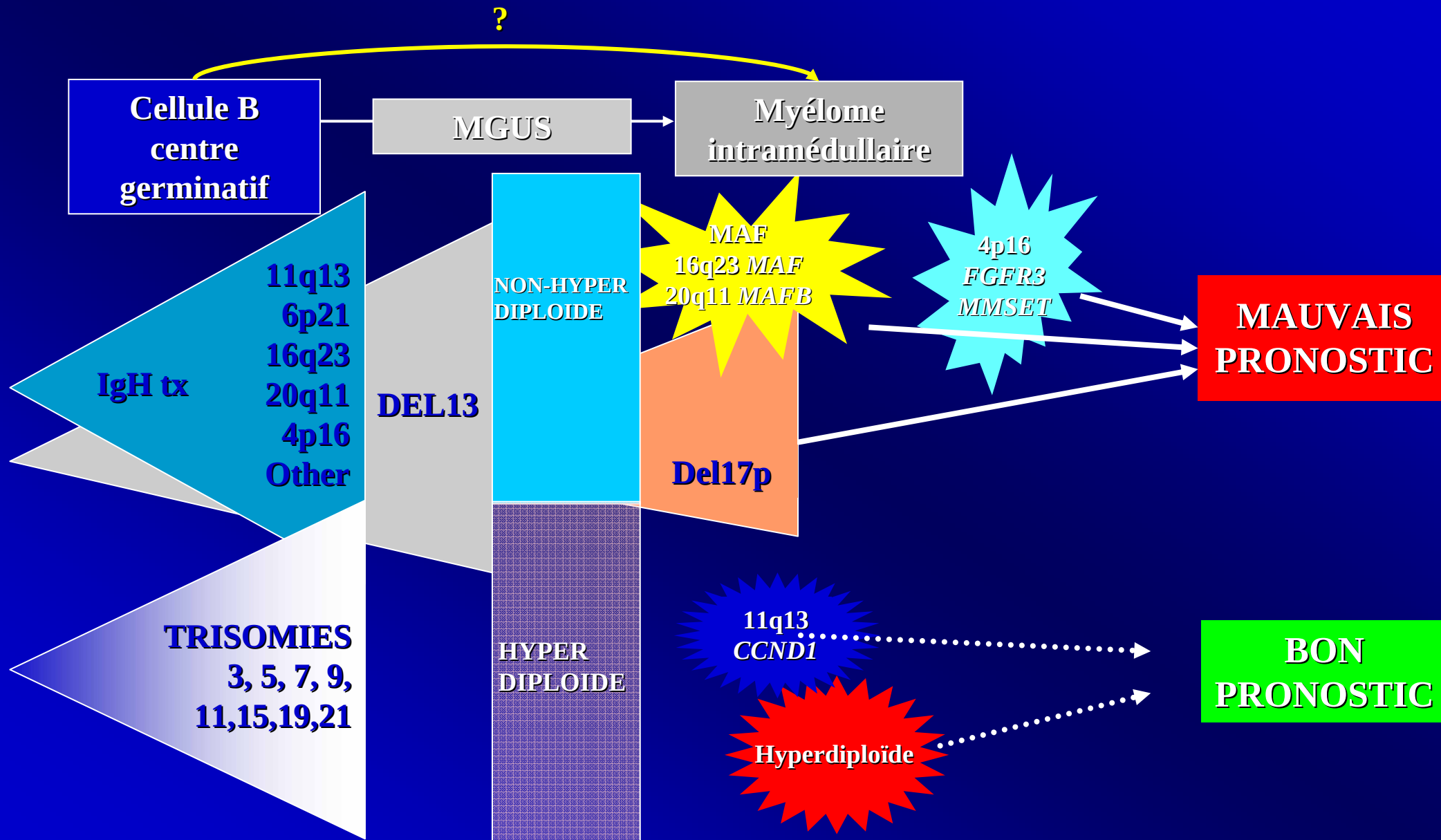
*Paramètres pris en compte dans la classification pronostique de Durie et Salmon

** Analyses réservées à des laboratoires spécialisés

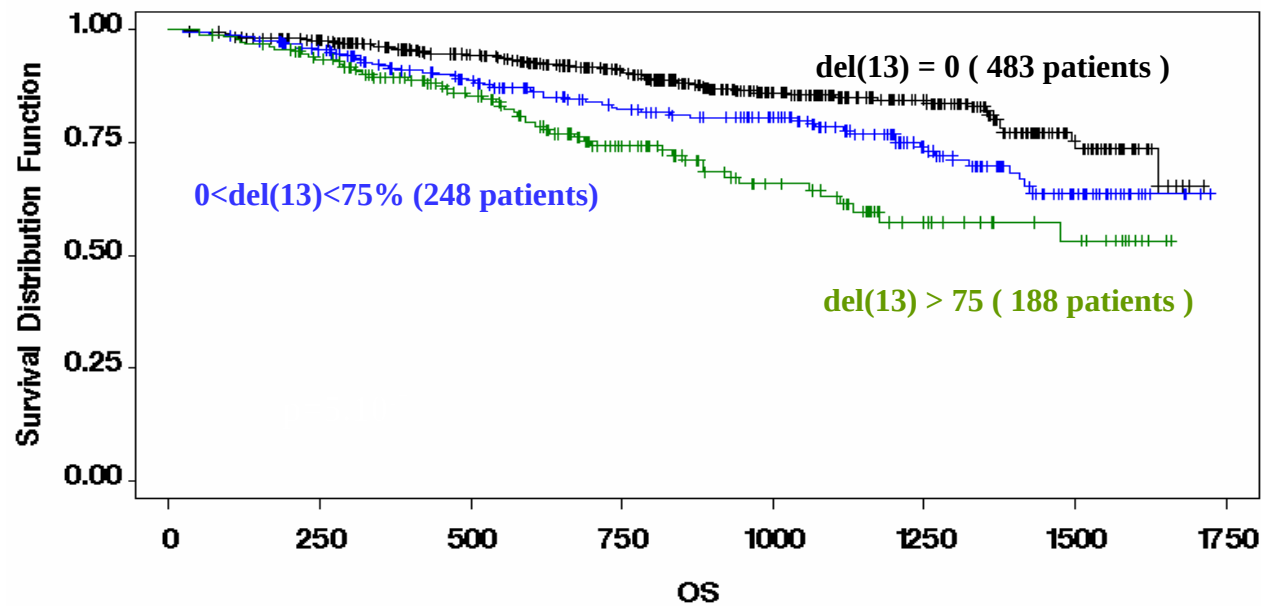
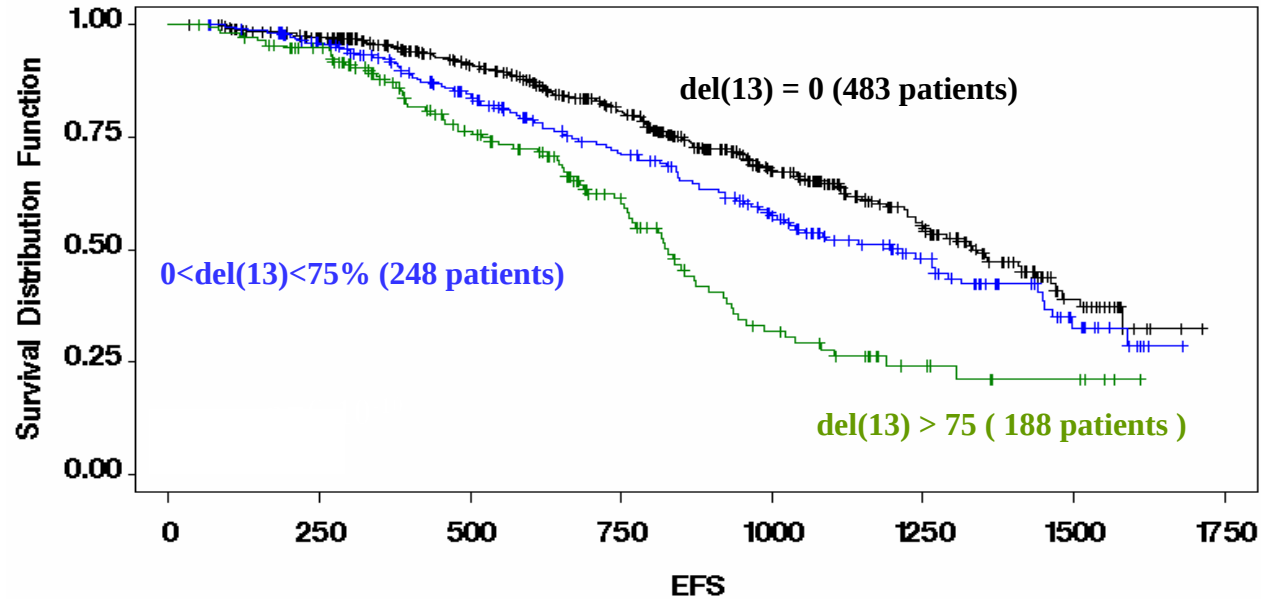
International Staging System (2003)

Stade	Paramètres	Survie médiane (mois)
1	$\beta 2m < 3,5 \text{ mg/L}$ et albumine $> 35 \text{ g/L}$	62
2	$\beta 2m > 3,5 \text{ mg/L}$ et albumine $< 35 \text{ g/L}$ ou $\beta 2 \text{ m } 3,5 \text{ à } 5,5 \text{ mg/L}$	44
3	$\beta 2m > 5,5 \text{ mg/L}$	29

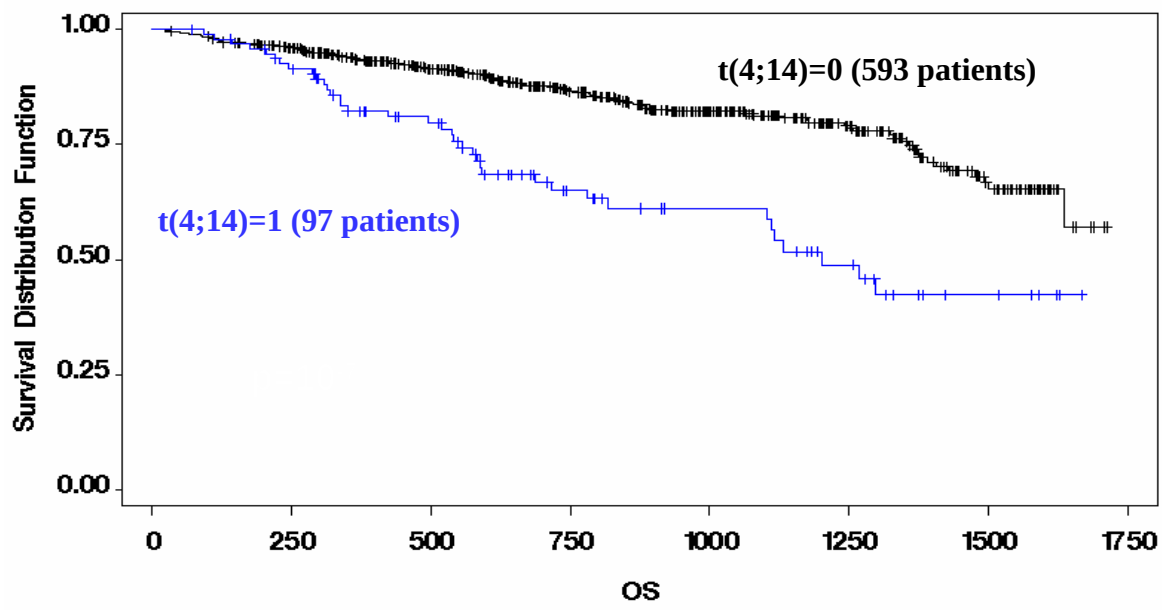
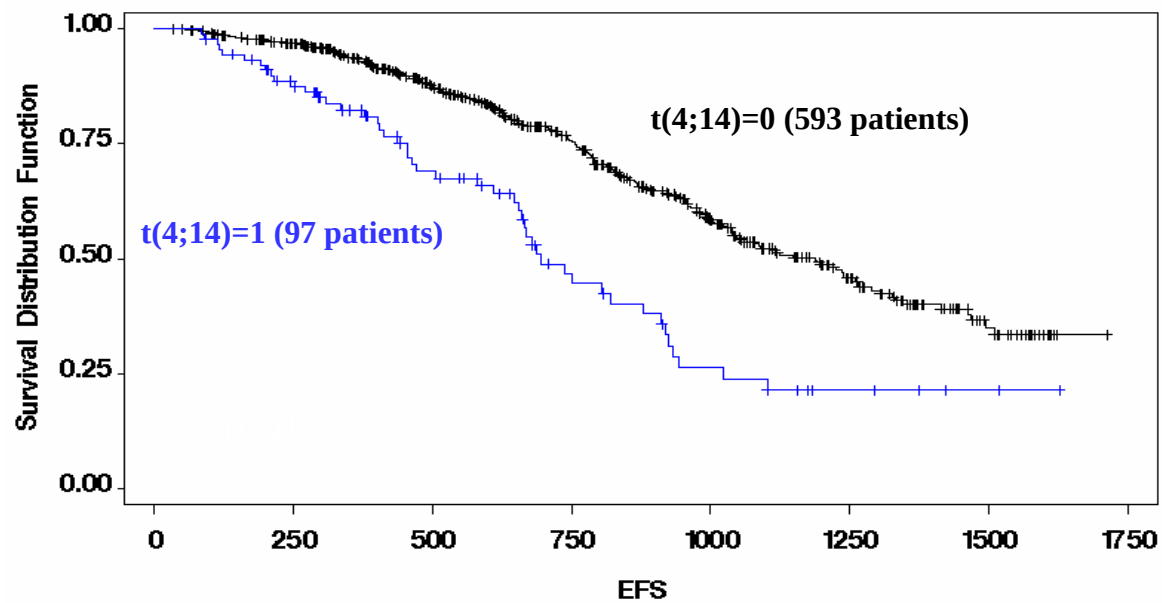
Oncogénèse



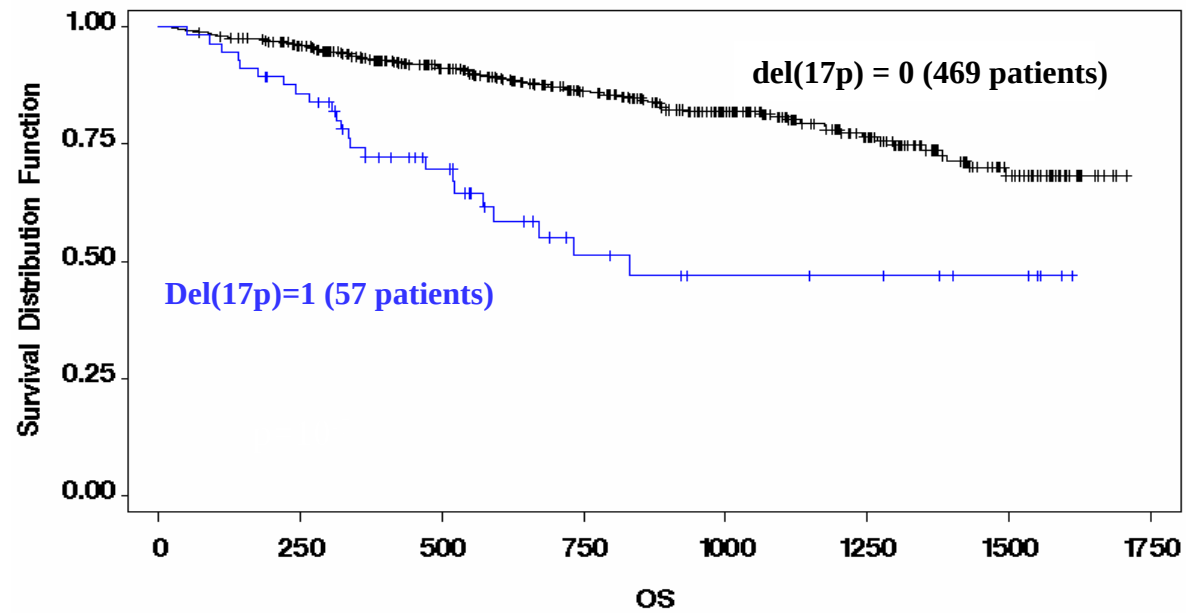
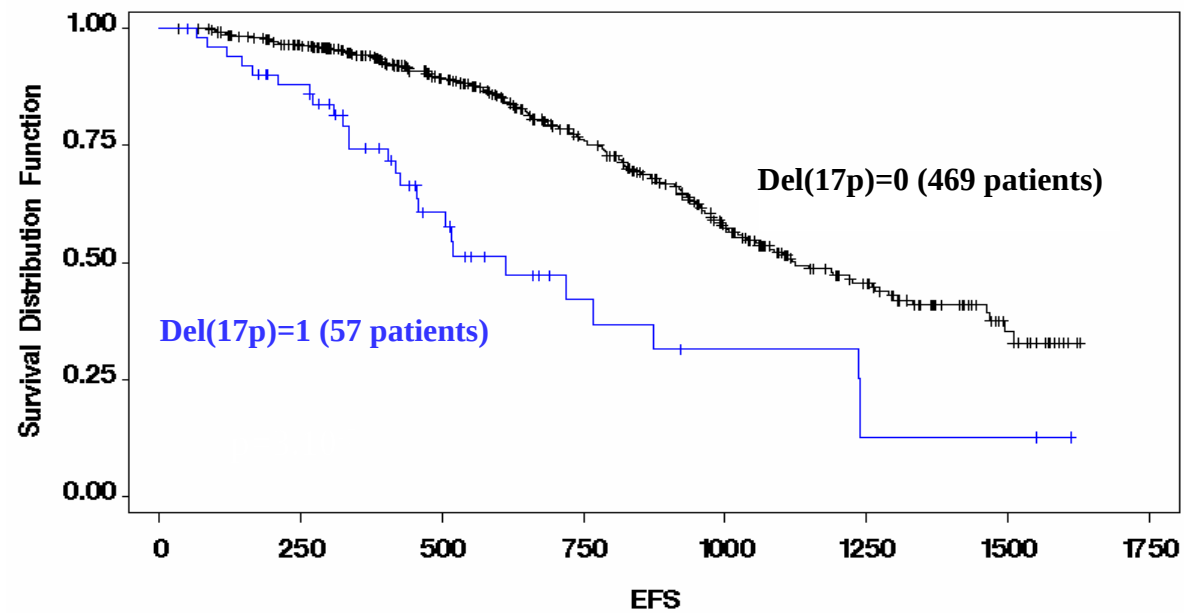
Del(13)



$t(4;14)$



Del(17p)



Survie t(4;14) ou del(17p)

