Modulation du remodelage osseux par les hormones intestinales

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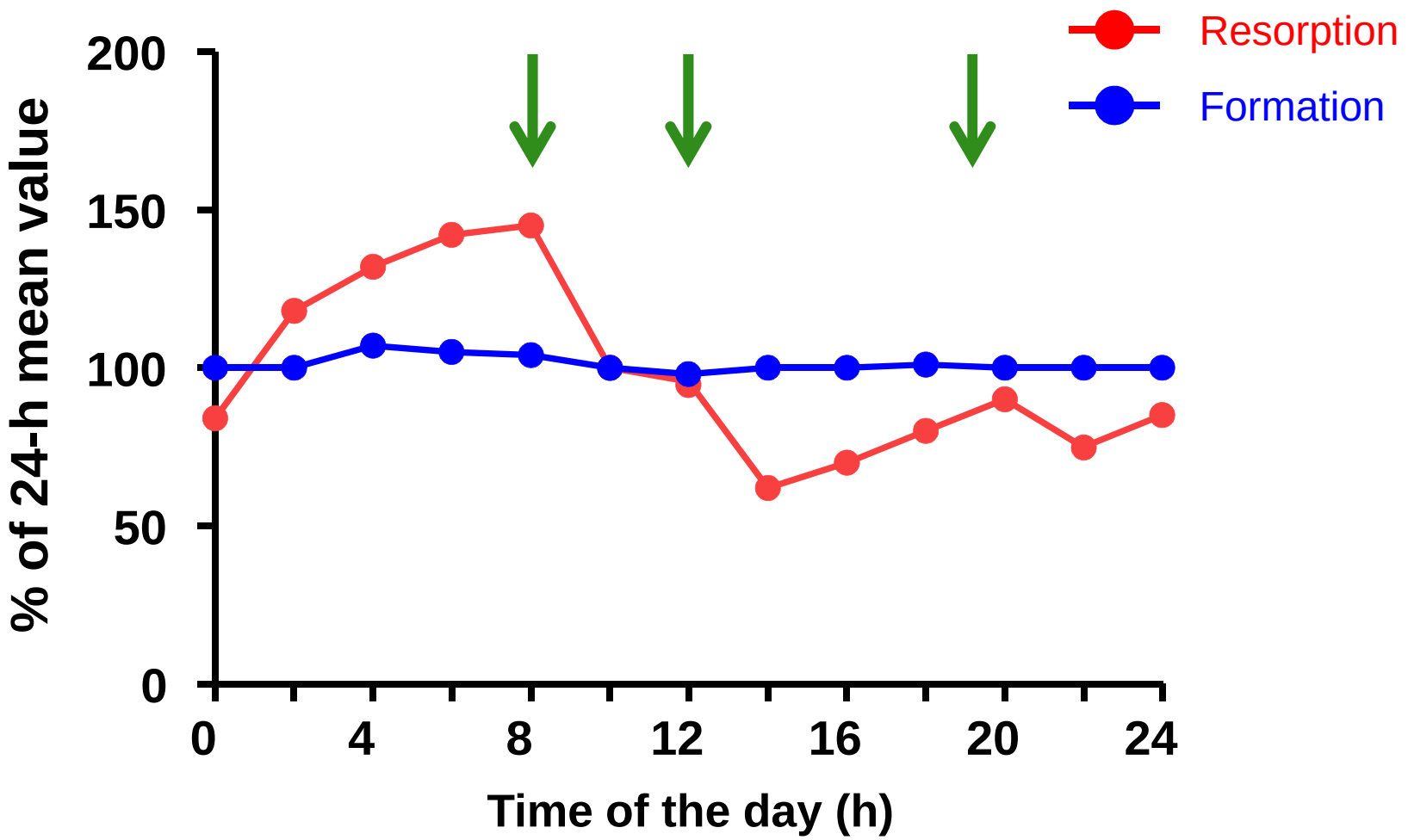
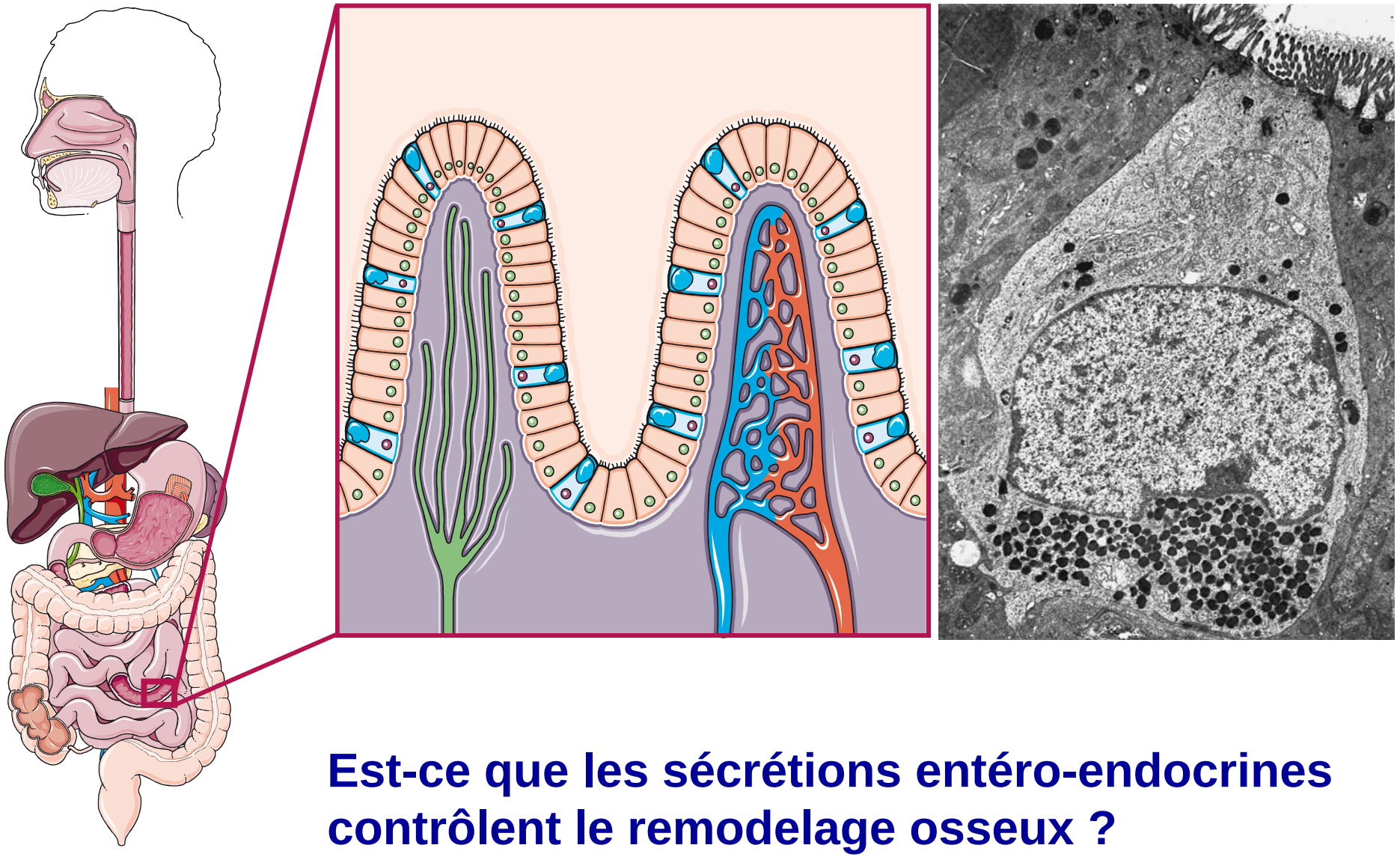
Evolution circadienne du remodelage osseux



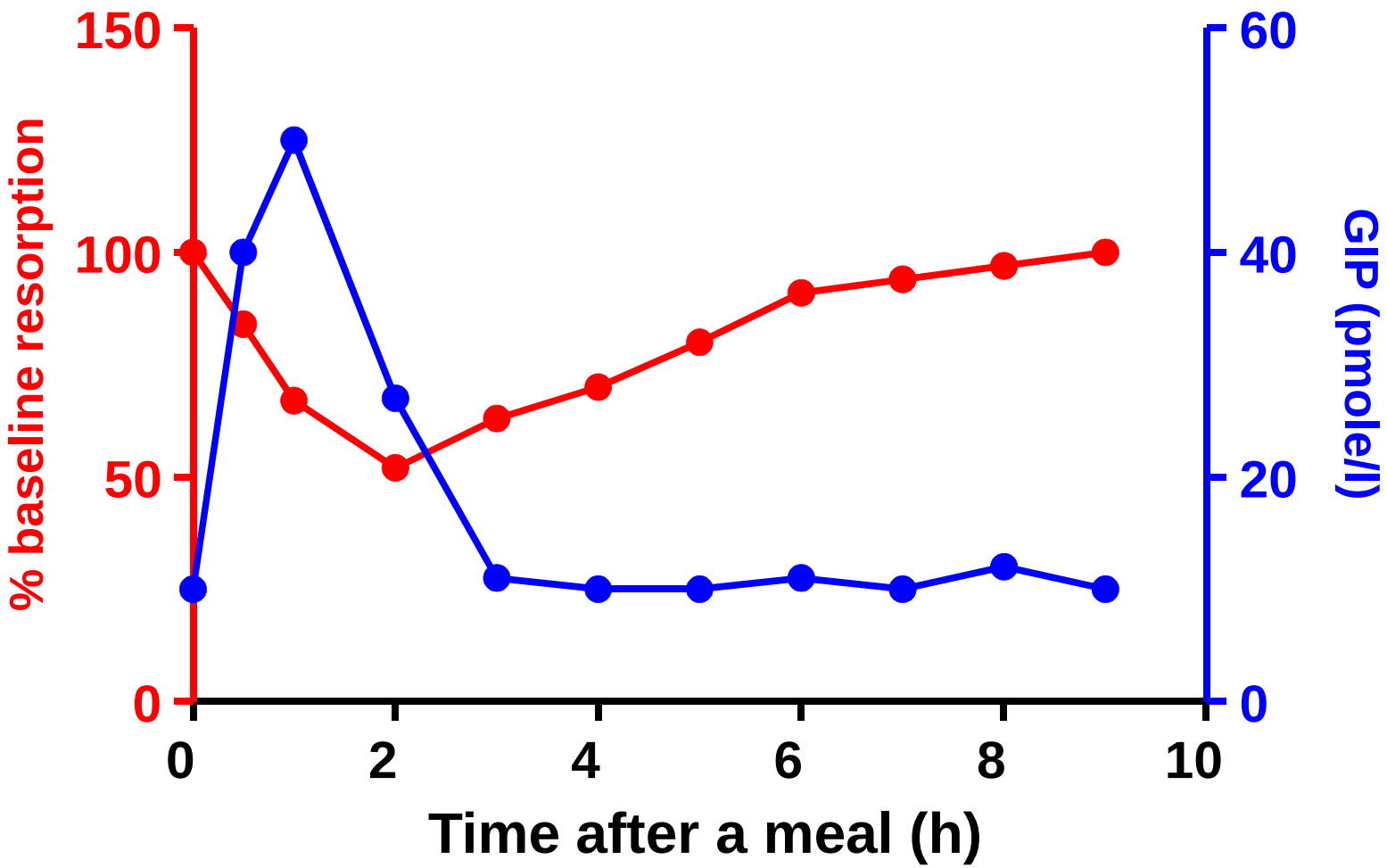
Adapted from Qvist et al., 2002, Bone 31: 57-61

Le système entéro-endocrine



Est-ce que les sécrétions entéro-endocrines contrôlent le remodelage osseux ?

Liens remodelage osseux – système entéro-endocrine



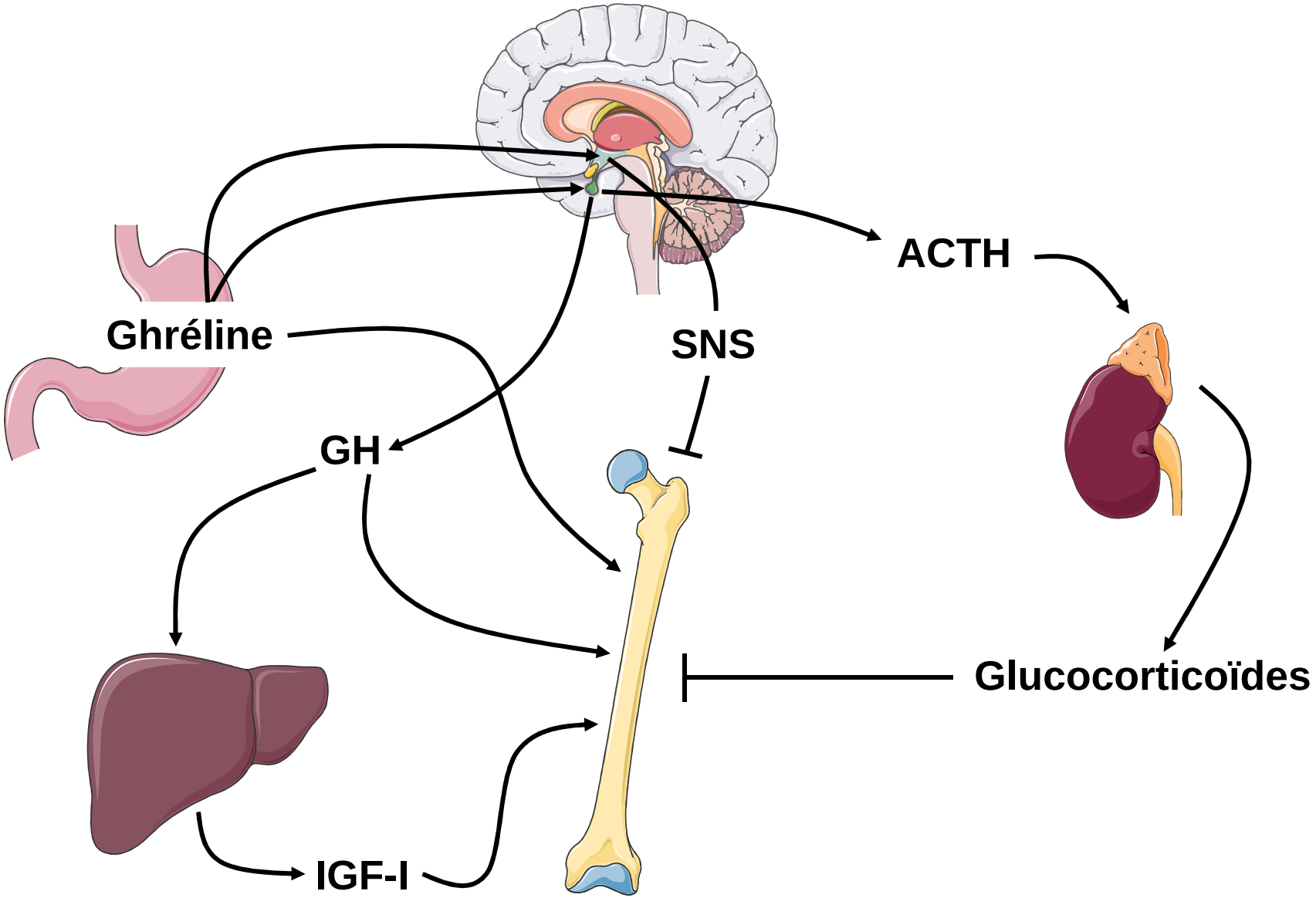
Adapted from Henriksen et al., 2003, JBMR 18: 2180-9

Le système entéro-endocrine

~12 cellules entéro-endocrines différentes
➔ 20 hormones

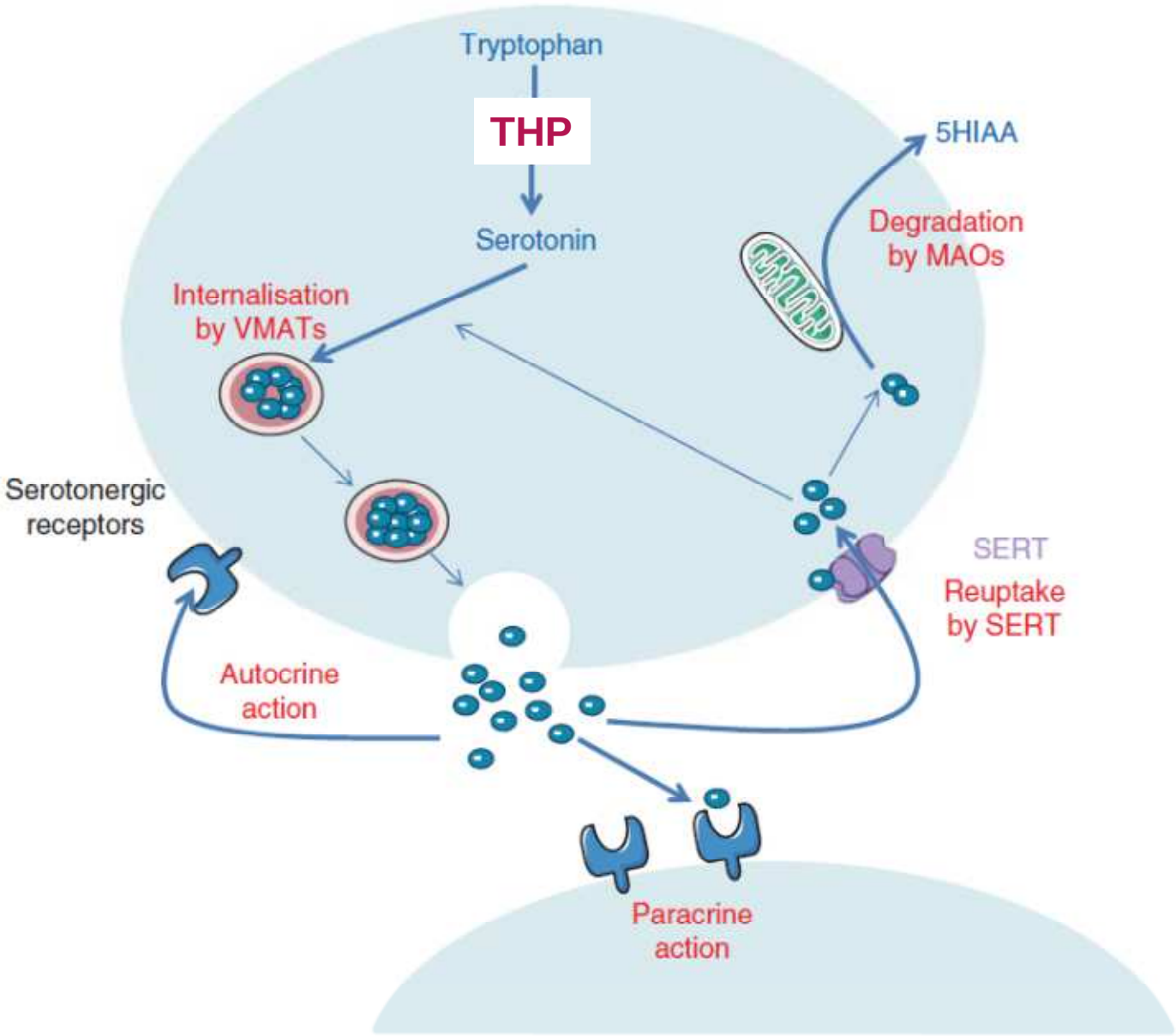
Ȼ entéro-endocrine	Hormones	Localisation
A	Ghréline	Estomac
K	GIP, Xénine	Duodénum
L	GLP-1, GLP-2	Iléon, colon
EC	Sérotonine	Estomac, intestin grêle, colon

Ghréline et physiologie osseuse

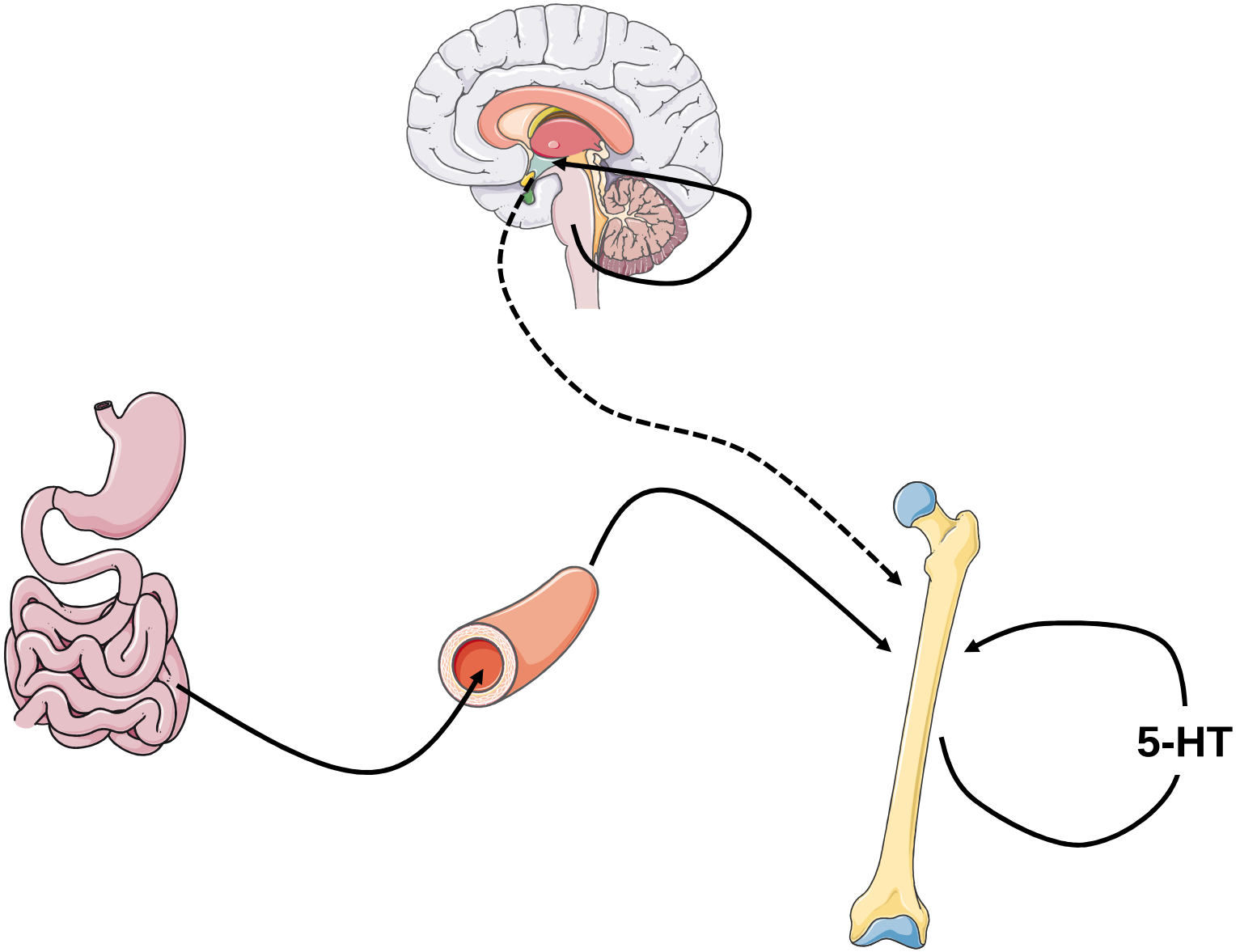


Adapted from Delhanty et al, Biofactors, 2014, 40: 41-8

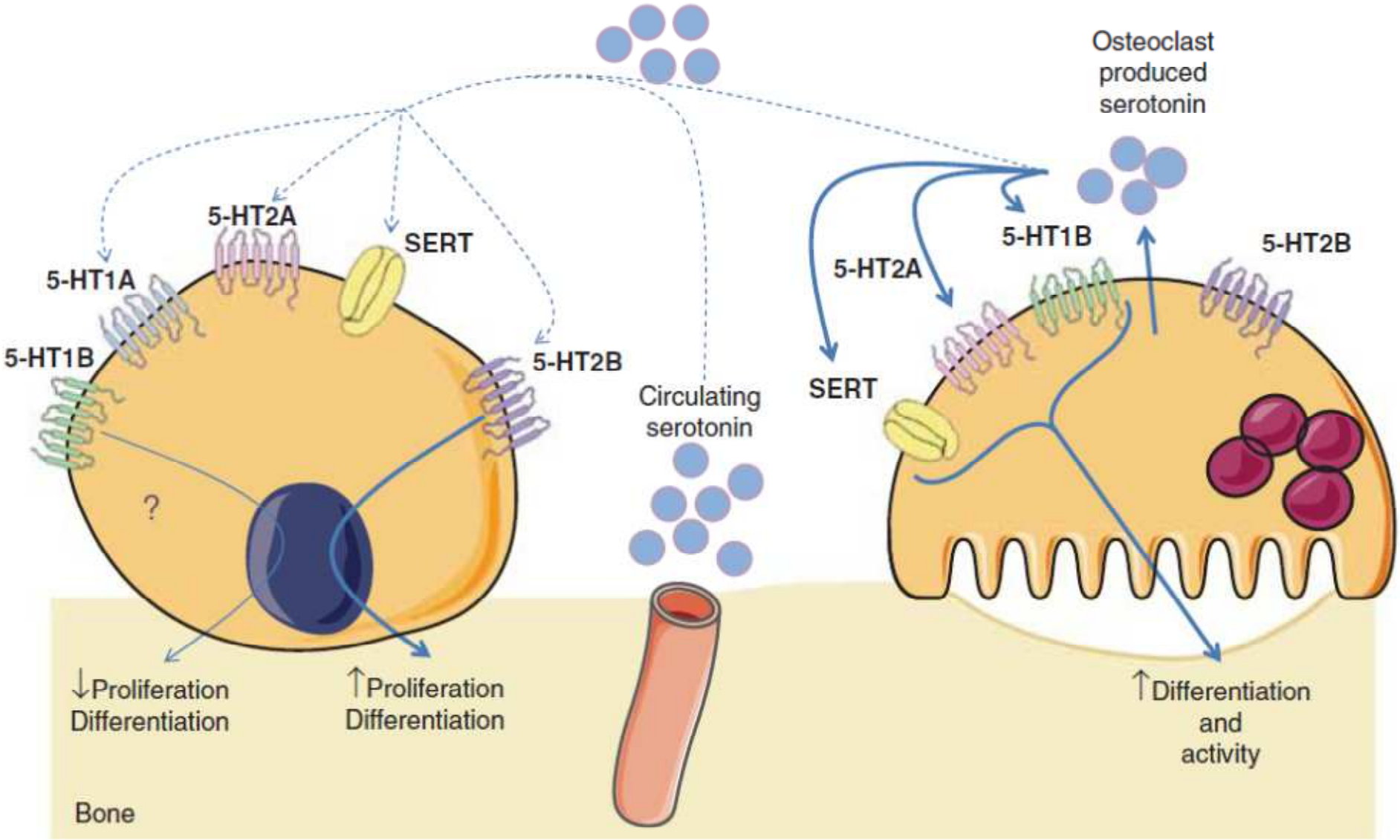
Sérotonine


Tryptophan
THP
Serotonin
5HIAA
Degradation
by MAOs
Internalisation
by VMATs
Serotonergic
receptors
SERT
Reuptake
by SERT
Autocrine
action
Paracrine
action

Relations sérotonine – Remodelage osseux



Rôles de la sérotonine



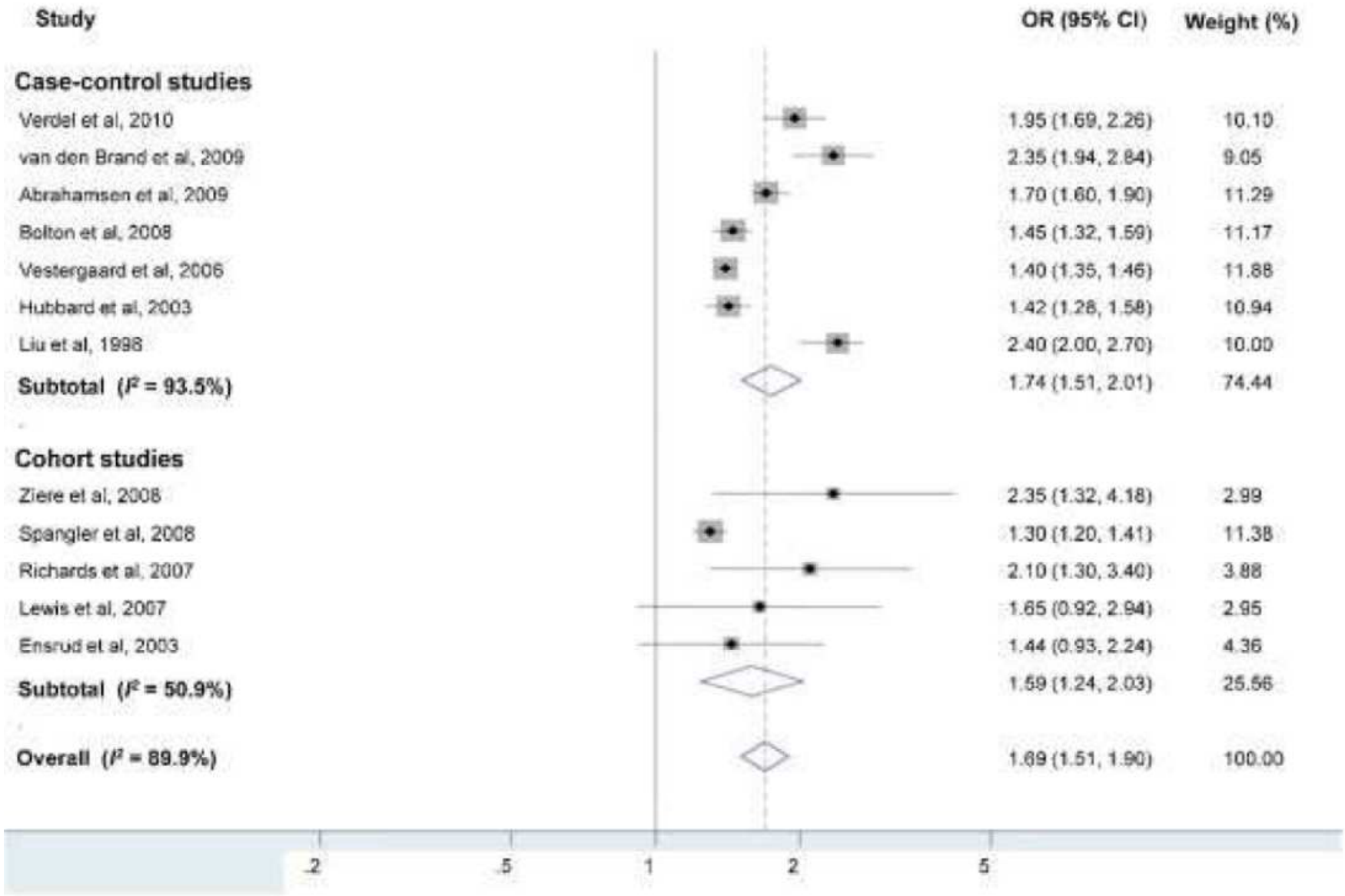
Sérotonine et DMO

MrOS Sweden study (Kristjansdottir et al, JBMR, 2018, 9: 1560-7)

Age (années)	75 (± 3)
IMC (kg/m2)	26 (± 4)
Fumeurs (%)	8
Sérotonine (µg/L)	149 (± 40)

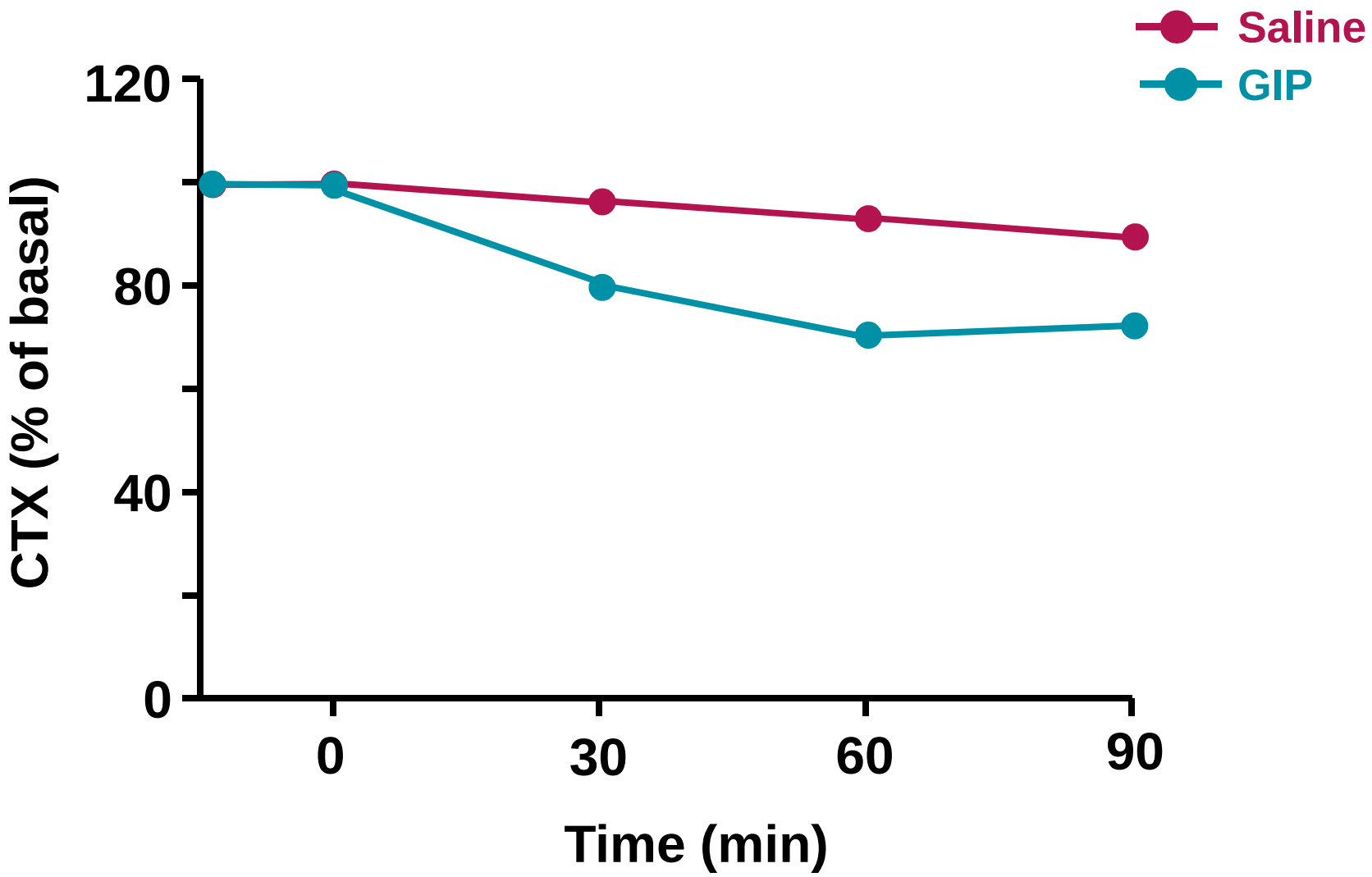
	Serotonin Q5 vs. Q1–4
All fractures, $n = 224$	
Age adjusted	1.50 (1.12–2.02)
Multivariable analysis[a]	1.38 (1.01–1.89)
Hip fractures, $n = 57$	
Age adjusted	2.62 (1.54–4.48)
Multivariable analysis[a]	2.30 (1.31–4.02)
Nonvertebral osteoporotic fractures, $n = 97$	
Age adjusted	2.07 (1.35–3.16)
Multivariable analysis[a]	1.82 (1.17–2.85)
Vertebral fractures, $n = 86$	
Age adjusted	1.07 (0.63–1.79)
Multivariable analysis[a]	1.35 (0.81–2.25)

Inhibiteur de la recapture de sérotonine et DMO



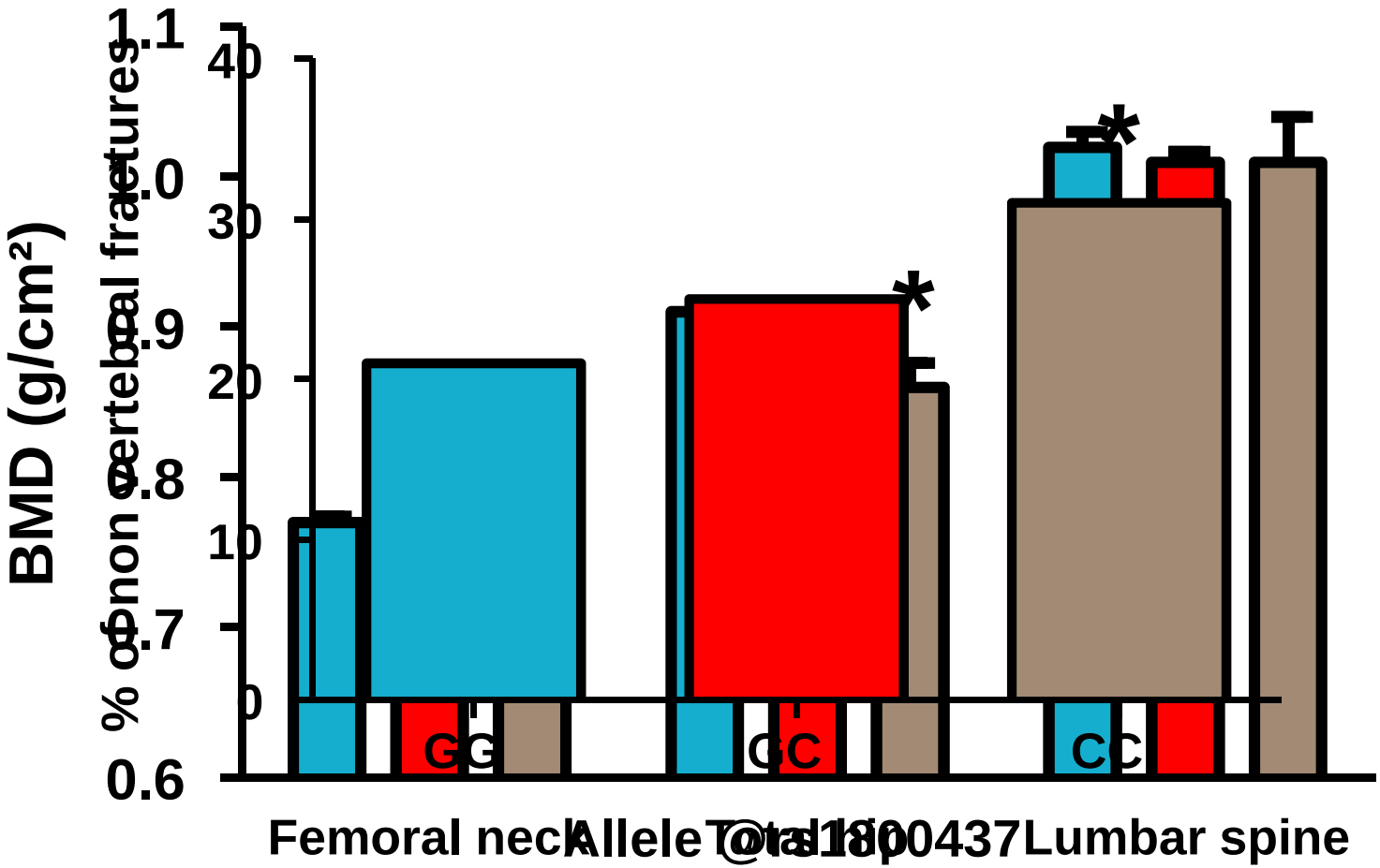
Adapted from Eom et al, JBMR, 2012, 27: 1186-95

Infusion GIP et remodelage osseux



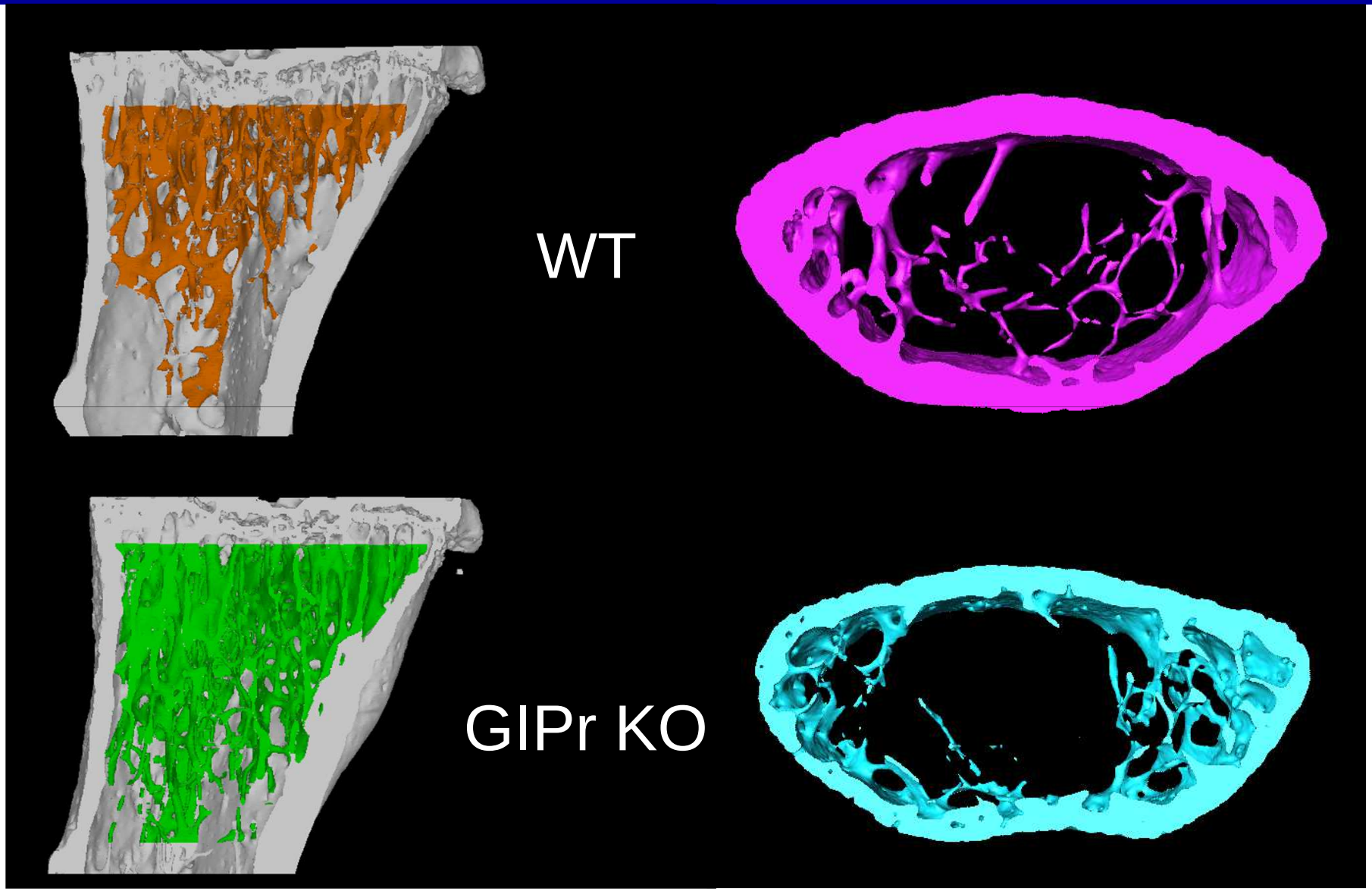
Adapted from Nissen et al, JCEM, 2014, 99: E2325-9

Polymorphisme GIPr et fragilité osseuse



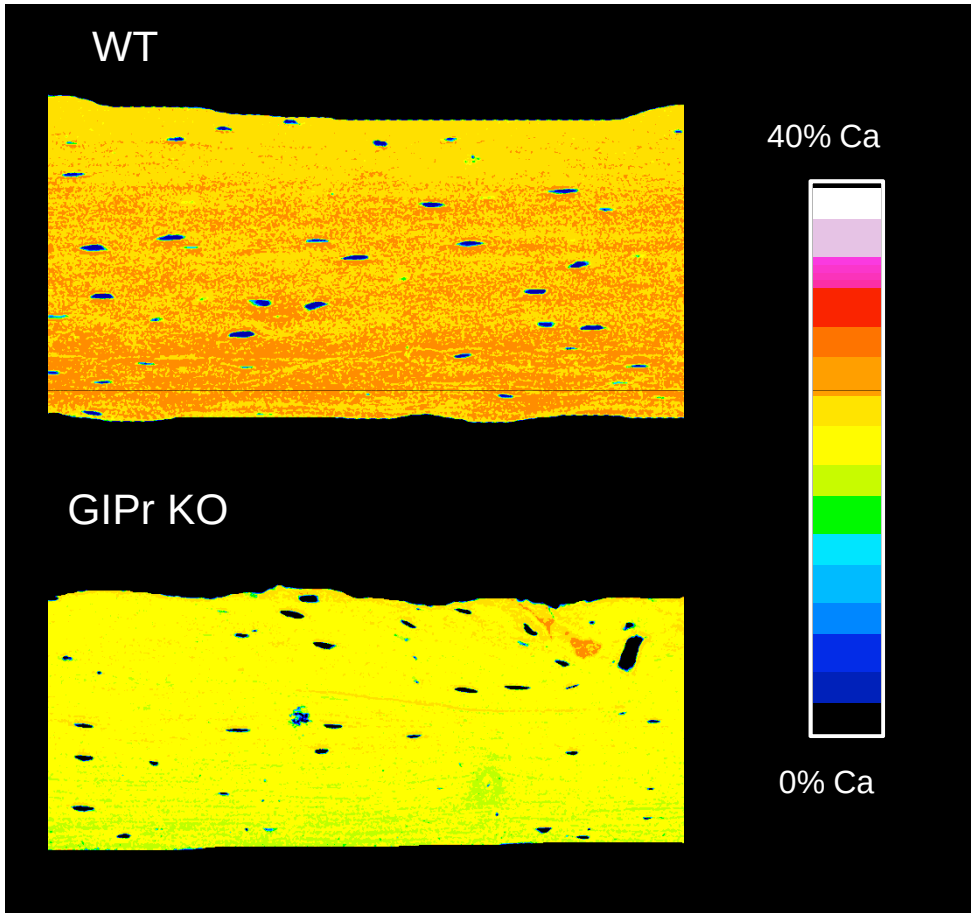
Adapted from Torekov et al, JCEM, 2014, 99: E729-33

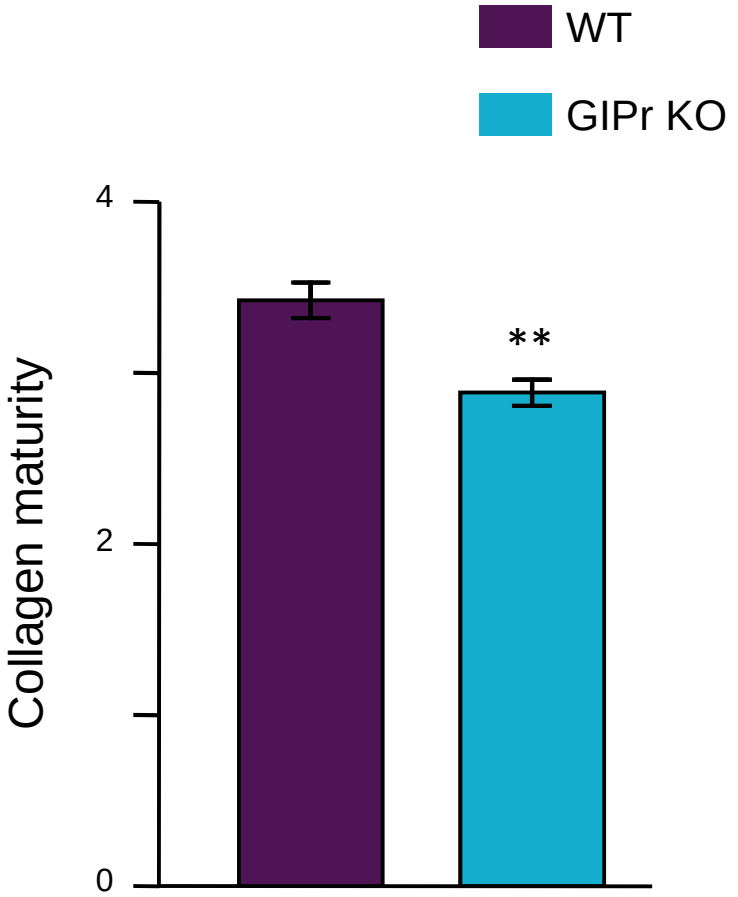
Relations GIP – microarchitecture osseuse



Adapted from Gaudain-Audrain, …, Mabilleau et al, Bone, 2013; Mieczkowska, …, Mabilleau et al, Bone, 2013

Relations GIP – composition osseuse

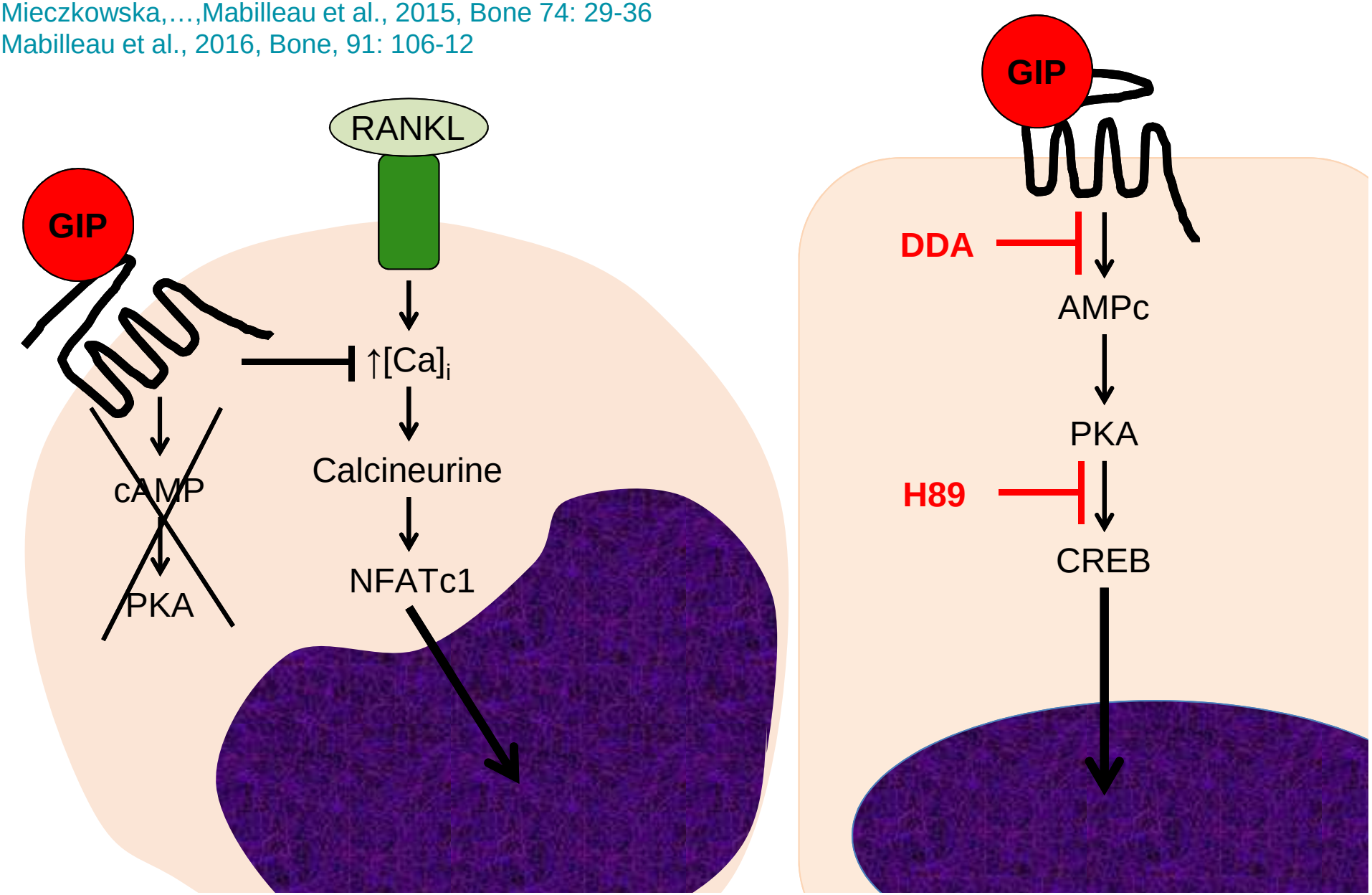




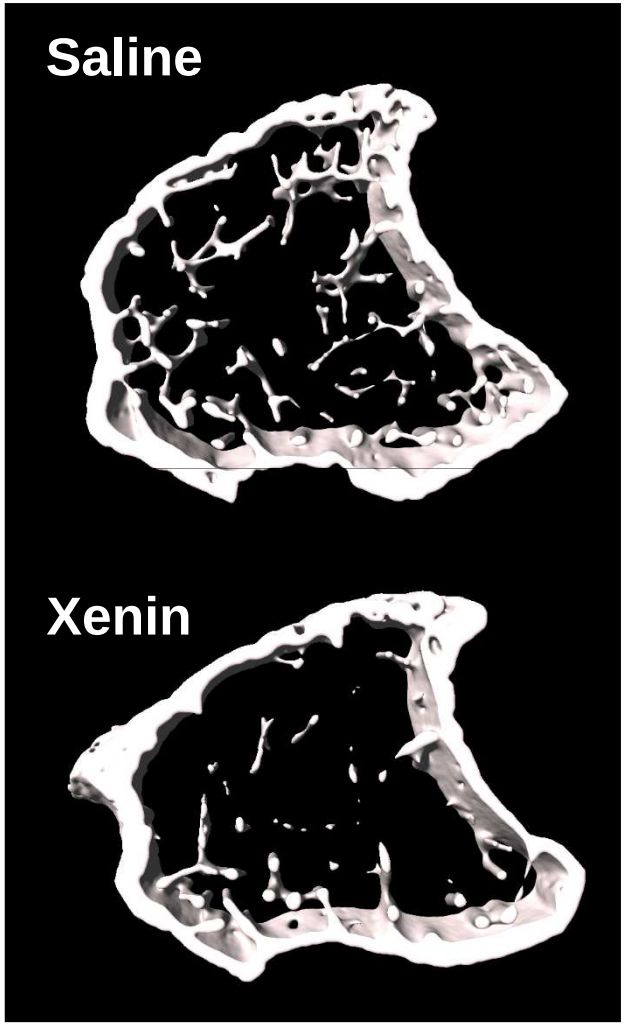
Mieczkowska,…,Mabilleau et al., 2013, Bone 56: 337-42

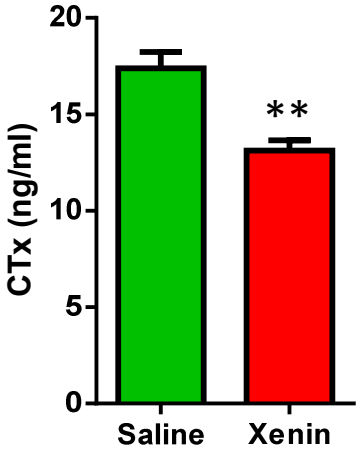
Relations GIP – cellules osseuses

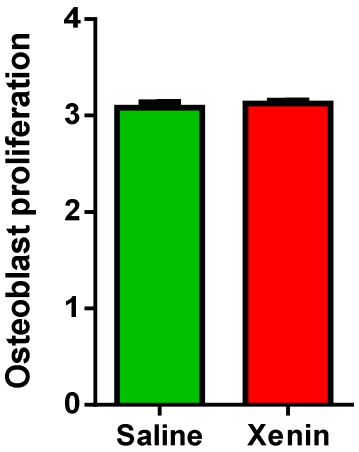
Mieczkowska,…,Mabilleau et al., 2015, Bone 74: 29-36
Mabilleau et al., 2016, Bone, 91: 106-12

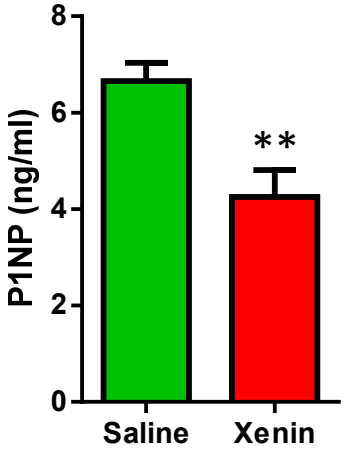


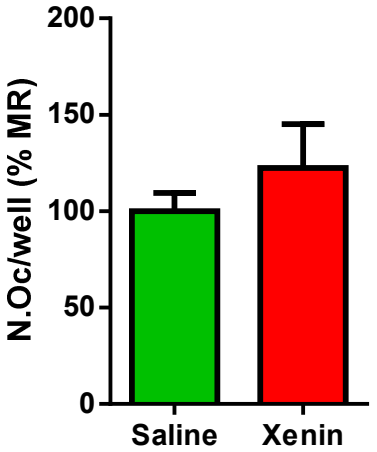
Relations xénine – tissu osseux





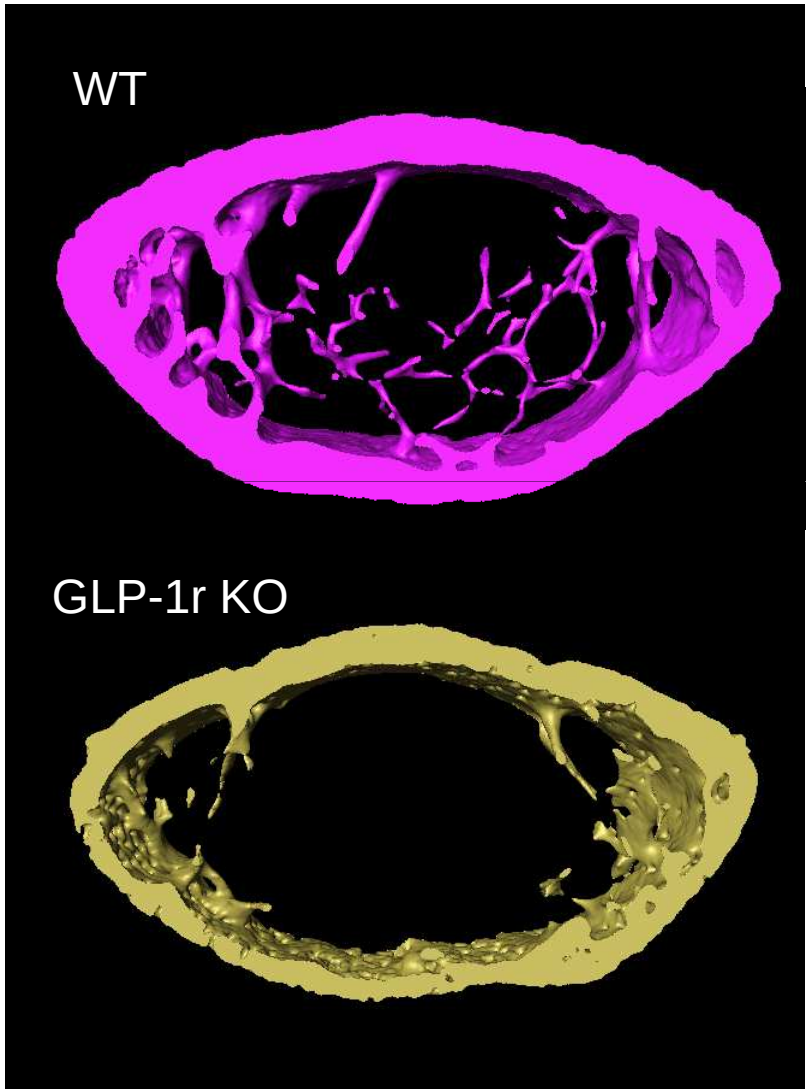


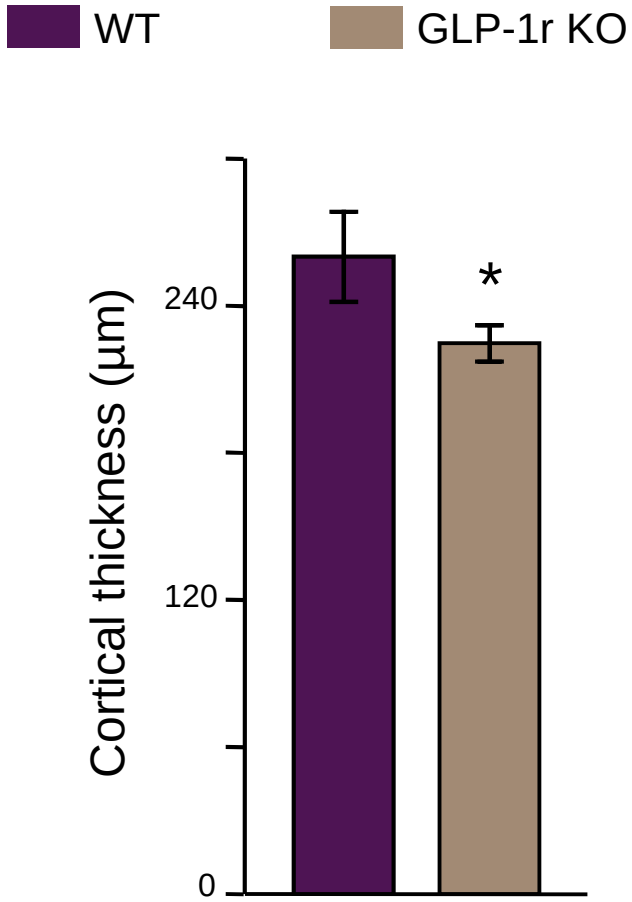




Travaux thèse Benoît Gobron 2017-2020

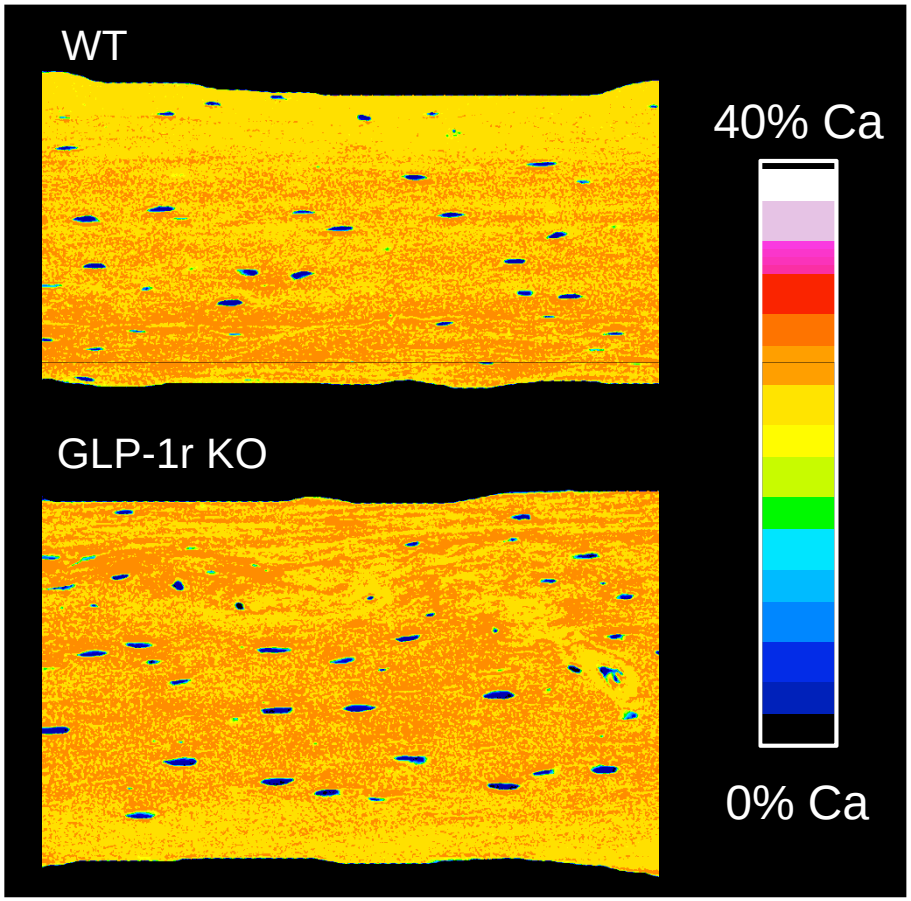
Relations GLP-1 – Microarchitecture osseuse

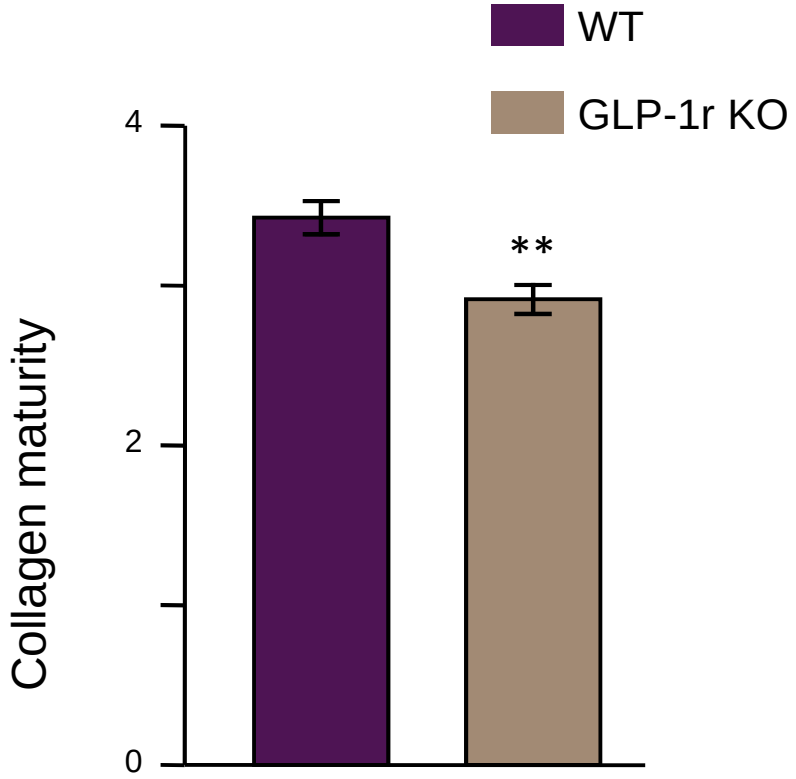




Mabilleau et al., 2013, J Endocrinol 219: 59-68

Relations GLP-1 – Composition osseuse

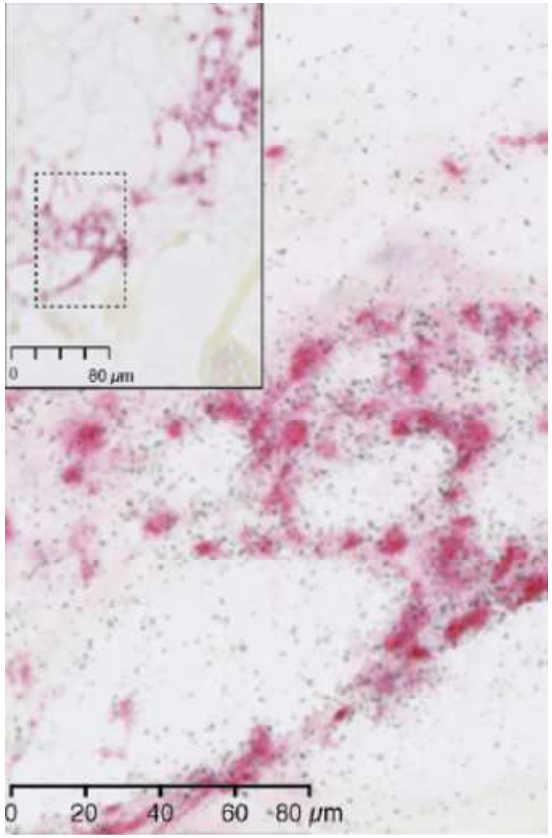




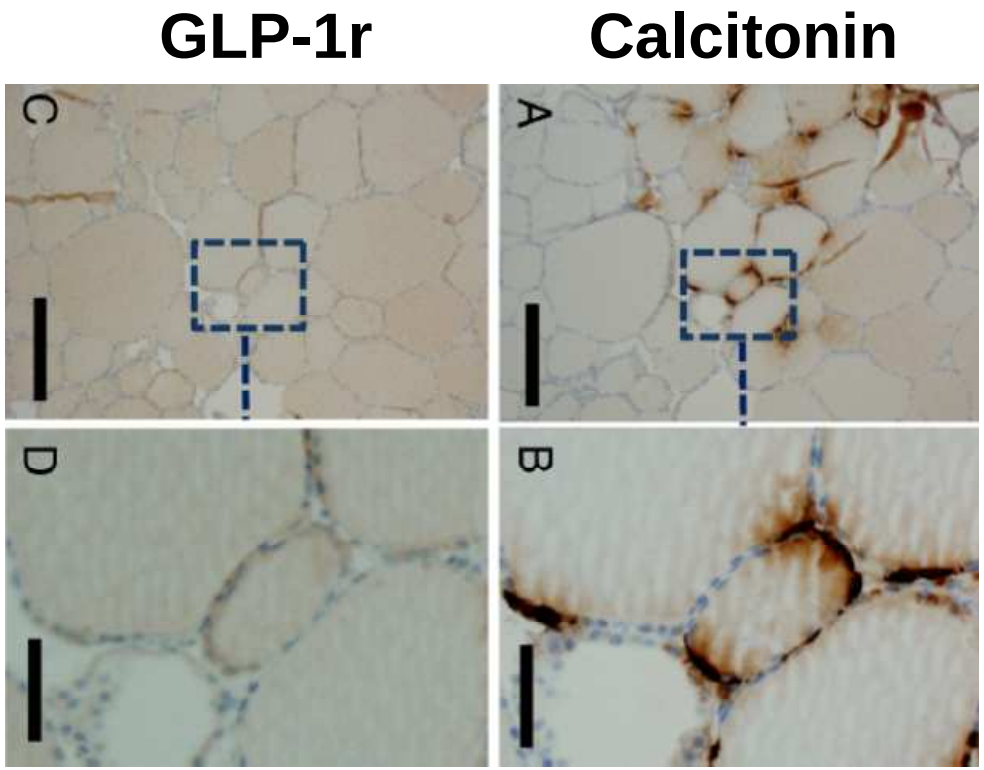
Mabilleau et al., 2013, J Endocrinol 219: 59-68

Relations GLP-1 – calcitonine

Rodents



NHP & humans

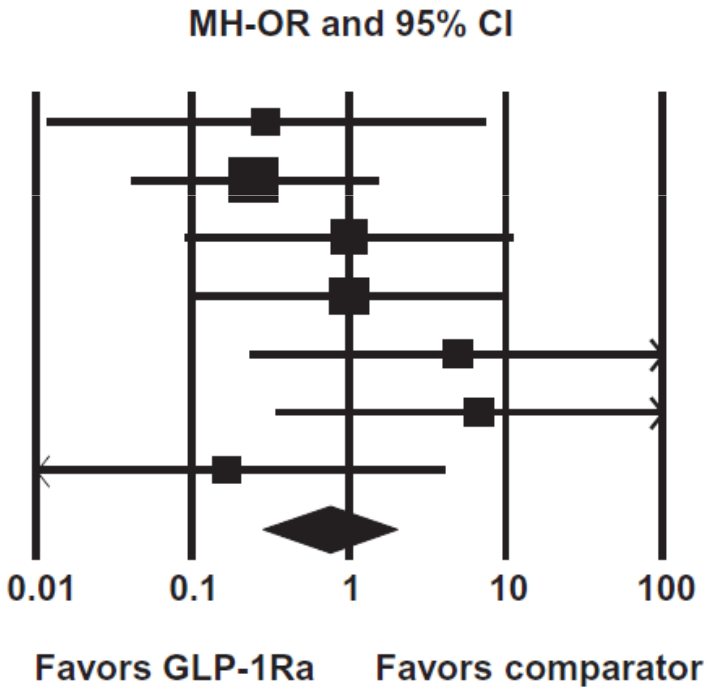


Madsen et al., 2012, Endocrinology, 153: 1538-47
Pyke et al., 2014, Endocrinology, 155: 1280-90

Relations agonistes GLP-1r – Fragilité osseuse chez l'homme

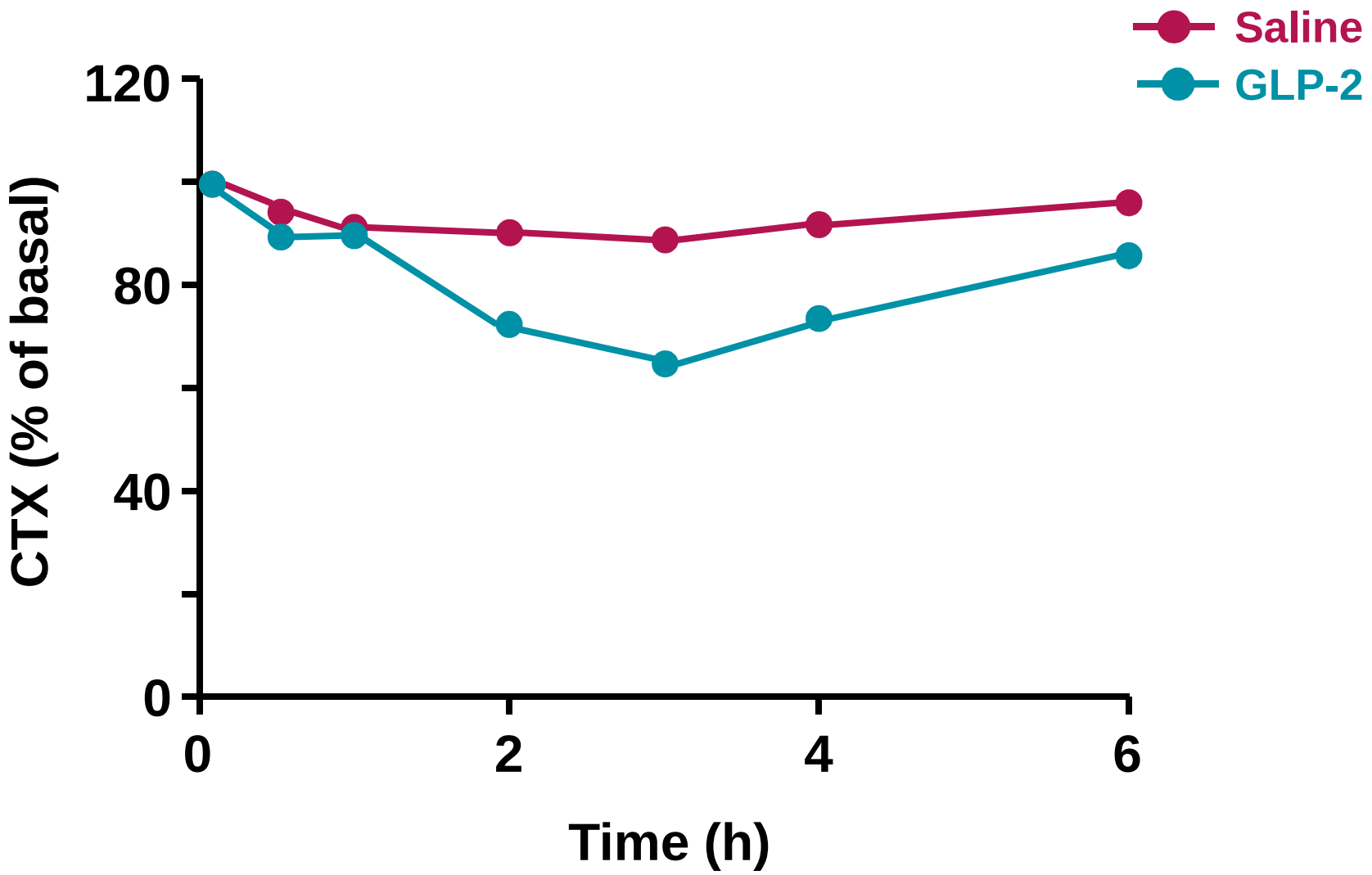
Meta-analysis of published RCT with duration ≥ 24 weeks

Study name	MH-OR	Lower limit	Upper limit	*Z*-value	*P*-value
Buse *et al.*[29]	0.295	0.012	7.298	-0.746	0.455
Nauck *et al.*[30]	0.248	0.041	1.497	-1.520	0.128
Garber *et al.*[31]	0.996	0.090	11.037	-0.003	0.997
Nauck *et al.*[30]	1.003	0.104	9.686	0.002	0.998
NCT00935532*	4.977	0.238	104.276	1.034	0.301
Gallwitz *et al.*[32]	6.604	0.349	132.694	1.265	0.206
Pratley *et al.*[33]	0.166	0.007	4.085	-1.099	0.272
	0.750	0.278	2.020	-0.570	0.569



Mabilleau et al., 2014, J Diabetes 6: 260-6

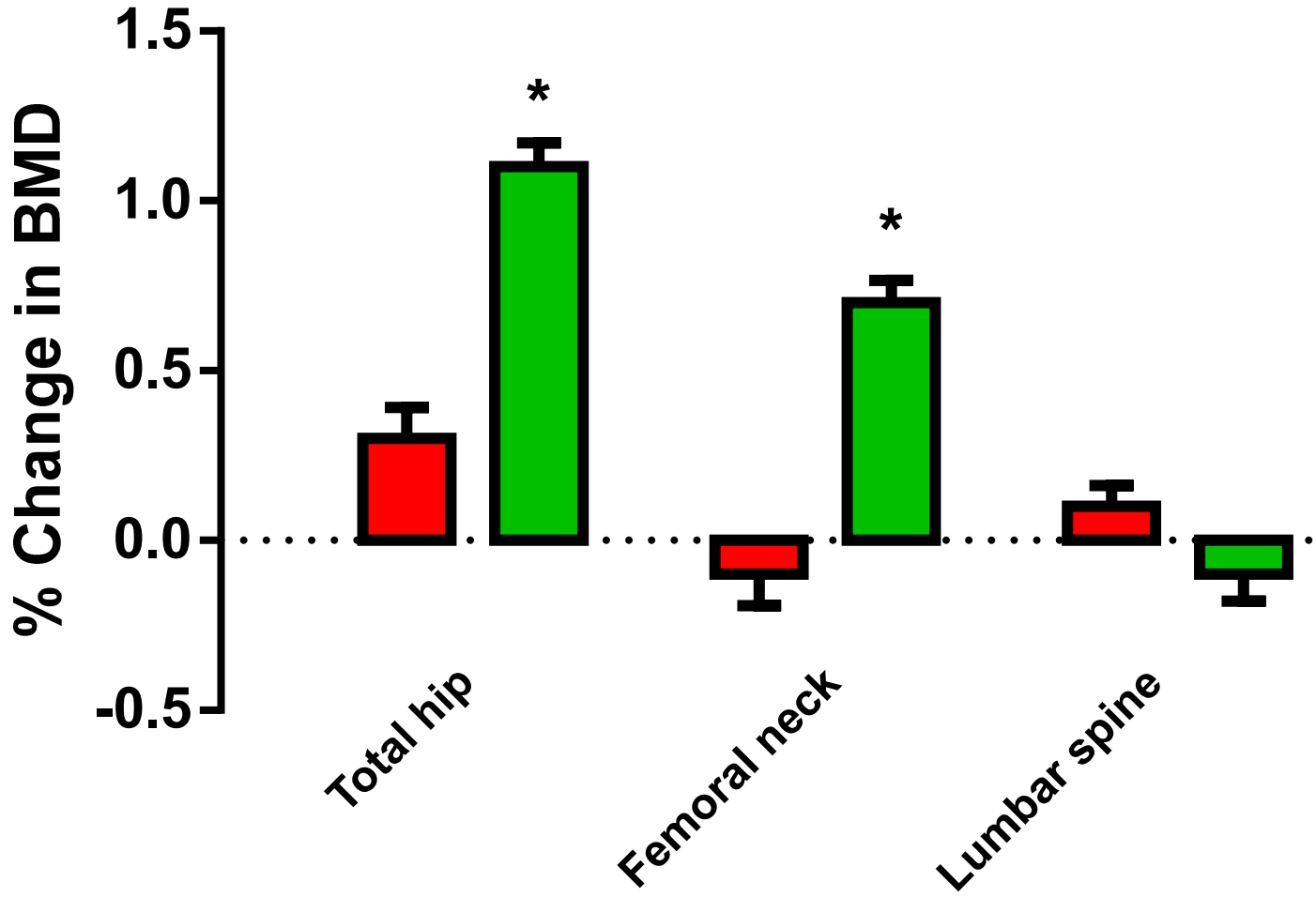
Infusion GLP-2 et résorption osseuse



Adapted from Henriksen et al, JBMR, 2003, 18: 2180-9

Relations GLP-2 et DMO

4 months teduglutide in post-menopausal women



Adapted from Henriksen et al, Bone, 2009, 45: 833-42

Conclusions