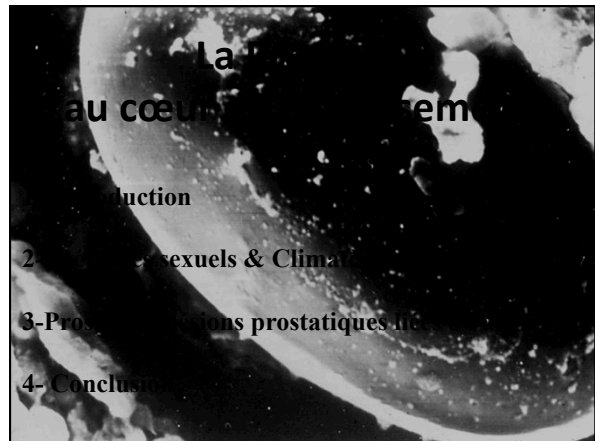


Vendredi 14 Novembre (9h-12h; pause; 14h-17h) Hôpital Tenon, à côté de l'amphithéâtre Béclère, salle ED4		
9h	Physiologie prostatique, vieillissement prostatique & sexuel chez l'homme	O. Cussenot
	Cancer de la prostate et l'homme (très âgé)	P. Mongiat-Artus
14h	Spécificités du traitement chirurgical de l'incontinence urinaire et du prolapsus de la femme âgée.	X. Deffieux
	L'imagerie spécifique en pelvi-périnéologie de la personne âgée	F. Boudghene



INTRODUCTION

Anatomie & Physiologie:

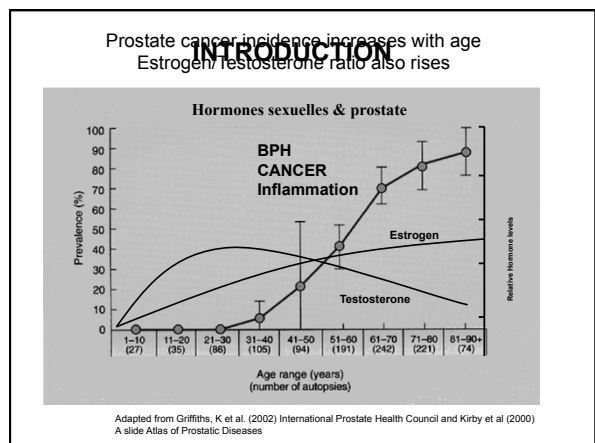
Carrefour uro-génital → Σ & Φ

Développement & Croissance androgéno-dépendante
→ Traitement

Variabilité morphologique lors du vieillissement

Épithélium glandulaire & mésenchyme fibro-musculaire
→ Cancer : Épithélium glandulaire (Zone périphérique)
& Hyperplasie Bénigne : Mésenchyme (Zone Transitionnelle)

Sécrétions androgéno-dépendantes (fluide séminal)
→ PSA (Prostate Specific Antigen)



La Prostate au cœur du vieillissement

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- 4- Conclusion

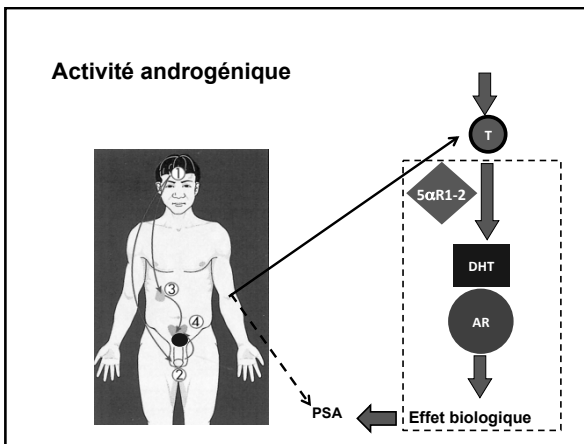
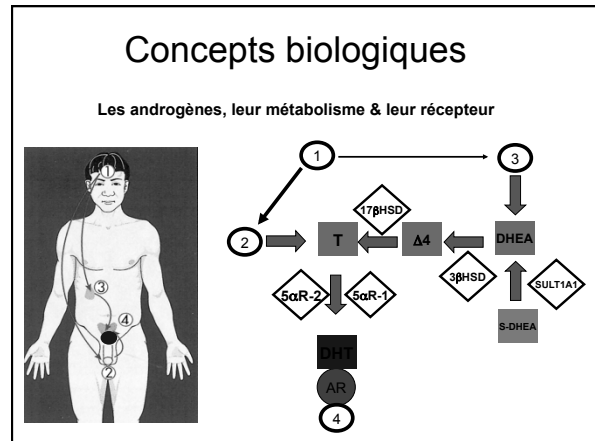
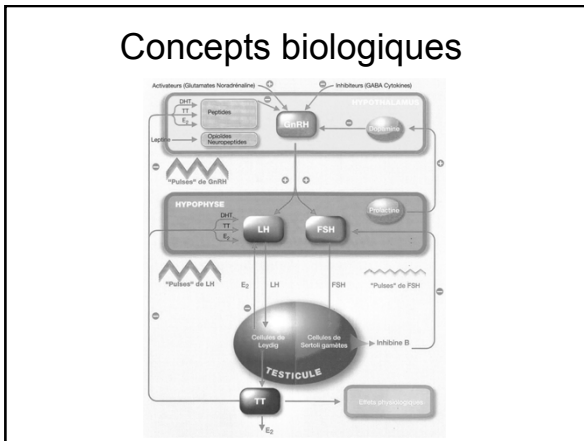
Concepts biologiques

Les H. Sexuelles, leur métabolisme & leur récepteur

ENDOCRINE

INTRACRINE

MOLECULAIRE



Mesure de l'activité androgénique

Albumine, SHBG

Totale / Biodisponible (Libre 2%)

→ Testostéronémie totale (>2,5ng/ml) (40 à 70% liée SHBG → inactive)

Variabilité SHBG++ (age, BMI, Tt, SNPs...)

→ Testostéronémie biodisponible

→ Activité biologique

Indirecte: Calculée: $[16,57 + 1,9 (SHBG-T)] \text{ nmol/l}$ ($y \text{ ng/ml} = x \cdot 0,2884 \text{ nmol/l}$)

Directe: Mesurée (>0,7ng/ml)

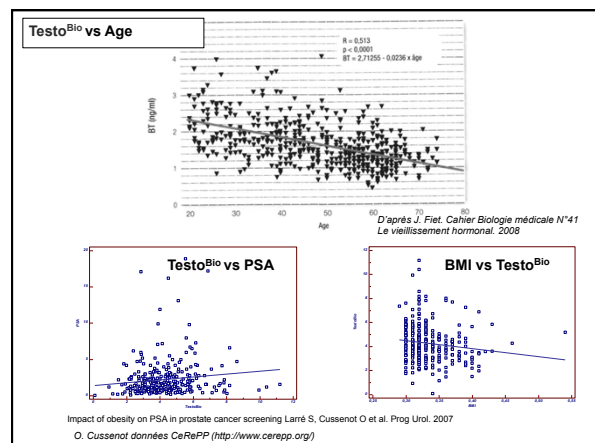
Mesure de l'activité androgénique

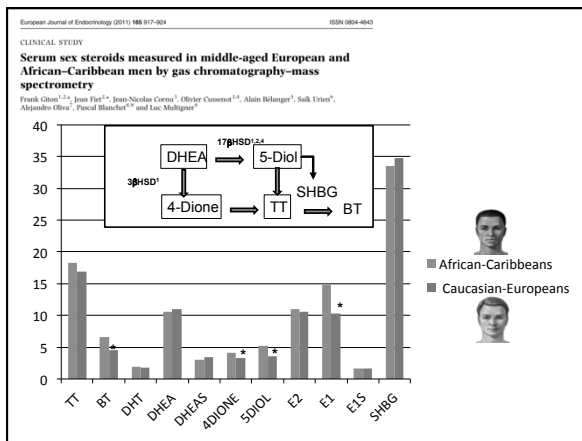
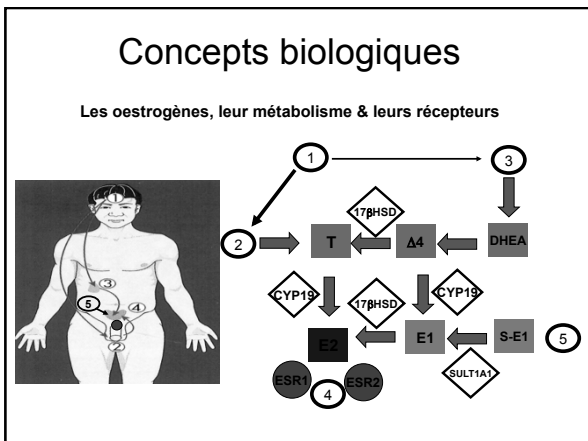
Partial Androgen deficit of the aging man

Score ADAM

	Non	Oui
Eprenez-vous une baisse de libido (désir sexuel)?	<input type="radio"/>	<input type="radio"/>
Eprenez-vous un manque d'énergie?	<input type="radio"/>	<input type="radio"/>
Eprenez-vous une diminution de force ou d'endurance?	<input type="radio"/>	<input type="radio"/>
La hauteur de votre taille a-t-elle diminué?	<input type="radio"/>	<input type="radio"/>
Avez-vous noté une diminution de la joie de vivre?	<input type="radio"/>	<input type="radio"/>
Etes-vous triste et/ou maussade?	<input type="radio"/>	<input type="radio"/>
Vos érections sont-elles moins fortes?	<input type="radio"/>	<input type="radio"/>
Avez-vous noté une altération récente de vos capacités sportives?	<input type="radio"/>	<input type="radio"/>
Vous endormez-vous après dîner?	<input type="radio"/>	<input type="radio"/>
Votre rendement professionnel s'est-il récemment dégradé?	<input type="radio"/>	<input type="radio"/>

+ Si « oui » N°3 ou N°7 + ou 3 Réponses « oui »





Men of African descent share biological features (genetic background) associated to more aggressive disease in caucasian men

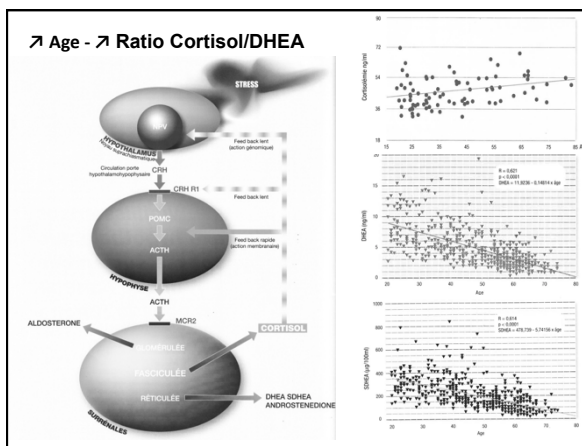
High Prevalence of susceptibility genetic markers 8q24 locus

Endocrine/intracrine profile Estrogens pathways bE2/CYP19

Combination of Polymorphisms From Genes Related to Estrogen Metabolism and Risk of Prostate Cancers: The Hidden Face of Estrogens
JOURNAL OF CLINICAL ONCOLOGY

Metastasis permissivity
METASTASIS KAI1/DARC
 Interaction of KAI1 on tumour cells with DARC on vascular endothelium leads to metastasis suppression
Bandyopadhyay, S. et al. Nature Med. 12, 935-938 (2006)

In Caucasian men loss of KAI1 expression in tumor cells & high expression of CYP19 In tumor microenvironment are poor prognosis factors independantly of Gleason Score

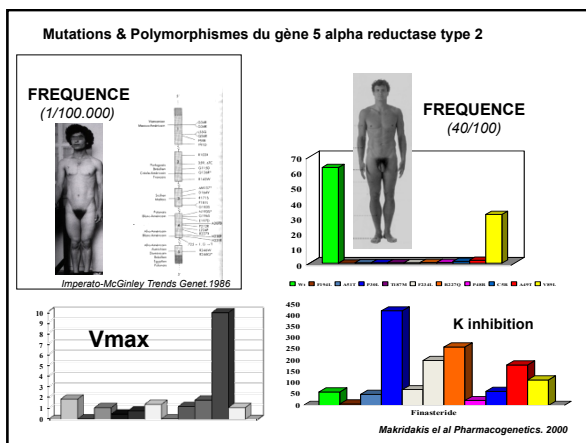
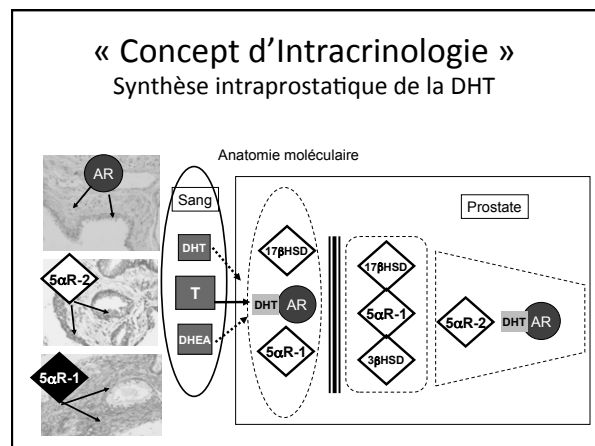
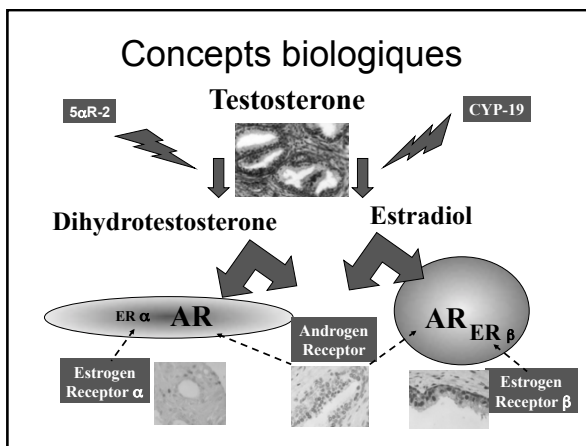
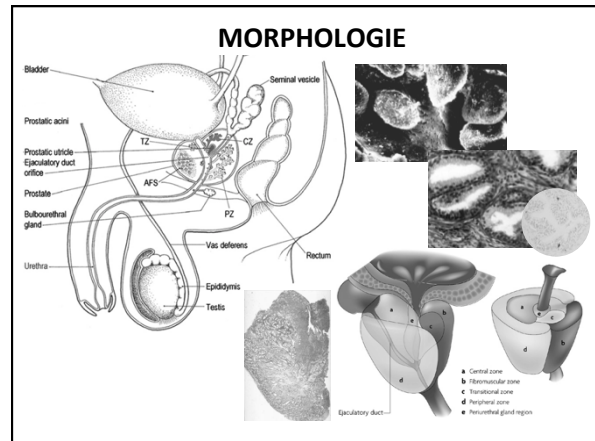
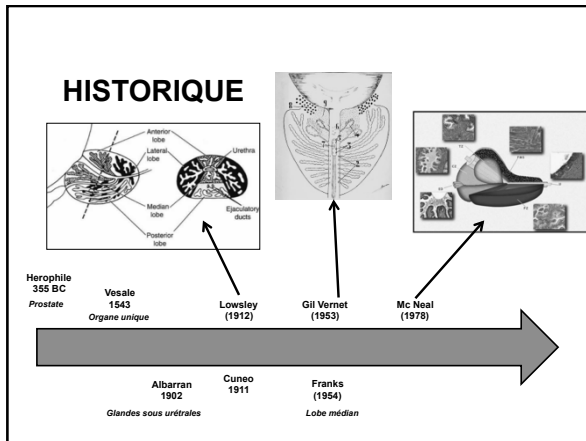


La Prostate au cœur du vieillissement

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La PROSTATE

De J. van CALCAR à A. WARHOL



Concepts expérimentaux

K.O.	Prostate
AR	0
SRD5A2	Vol. -
ESR1	Vol. -
ESR2	Vol. → Dysplasia
CYP19	Vol. -

DES → Vol. ↑, Dysplasia

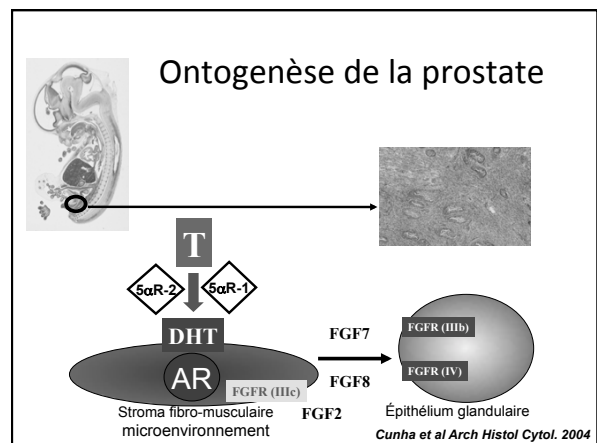
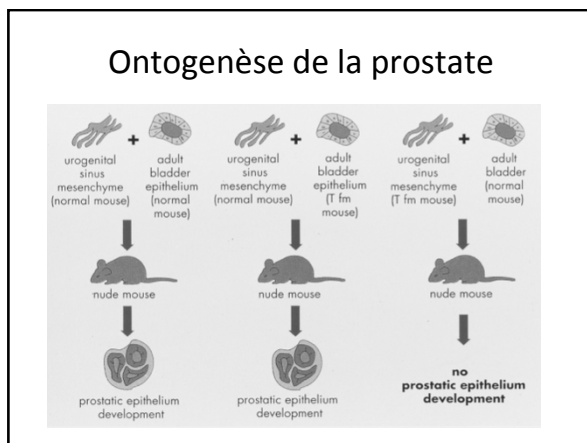
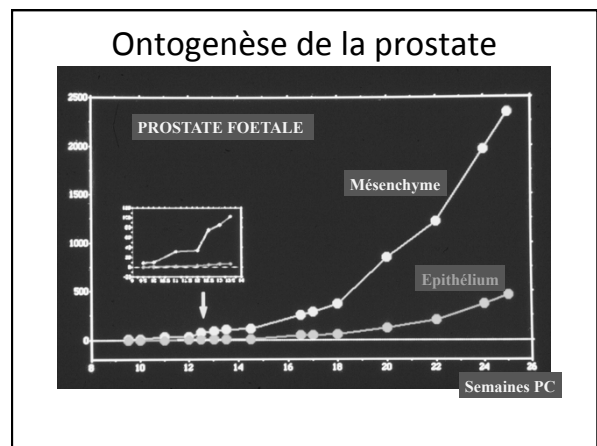
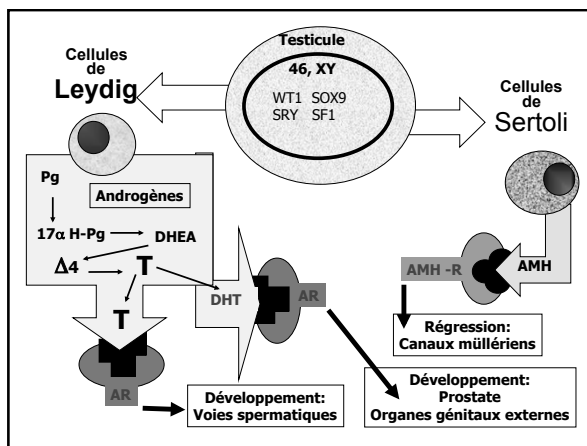
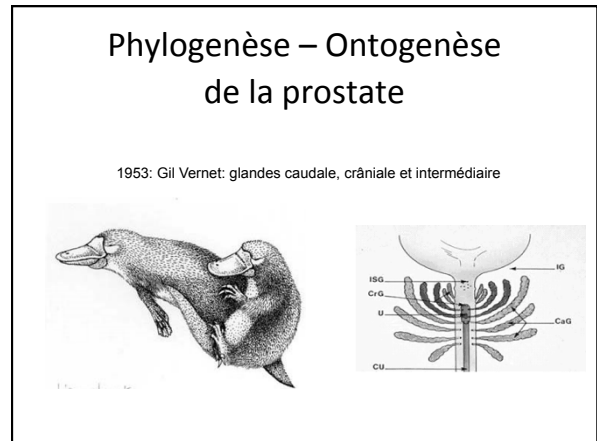
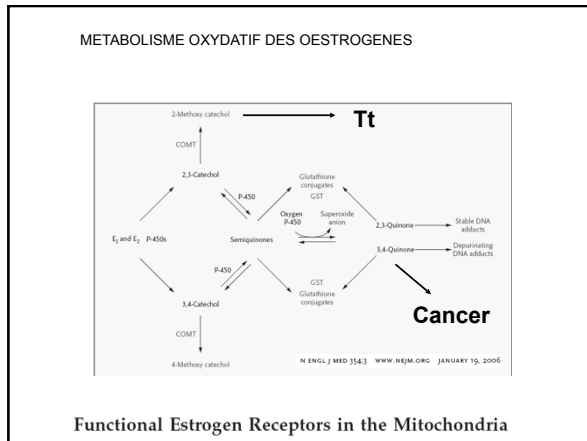
DES + ERaKO → Vol. →

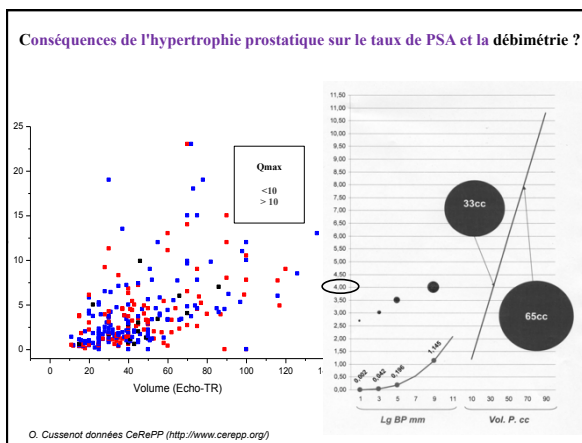
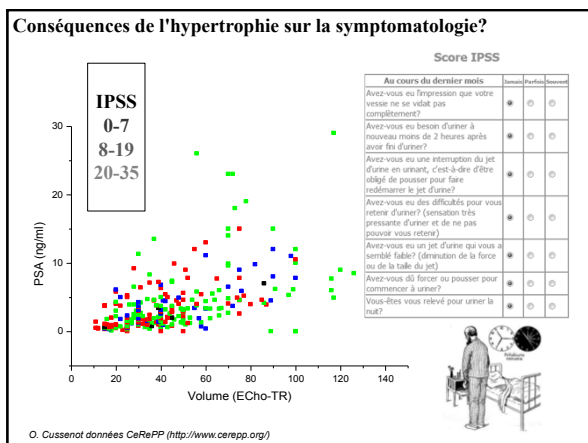
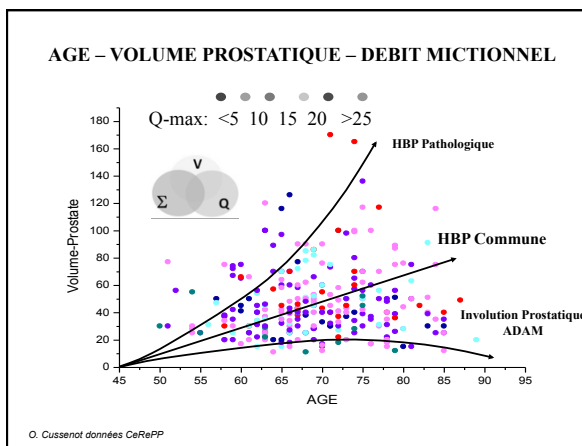
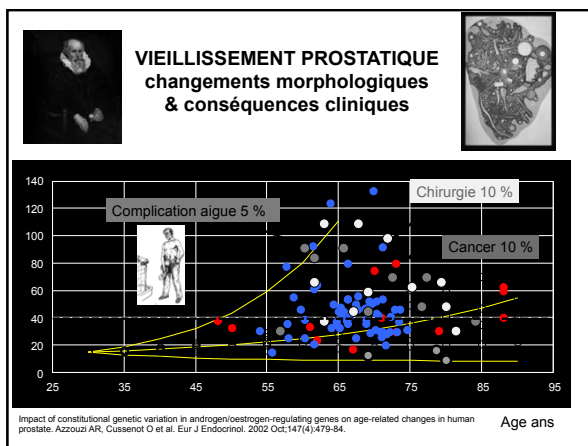
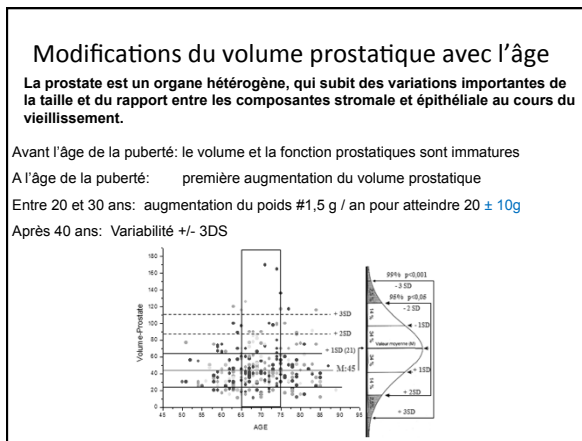
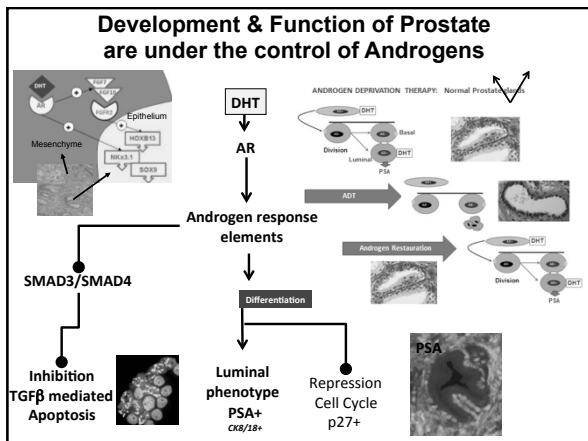
DES + ERbKO → Vol. ↑, Dysplasia

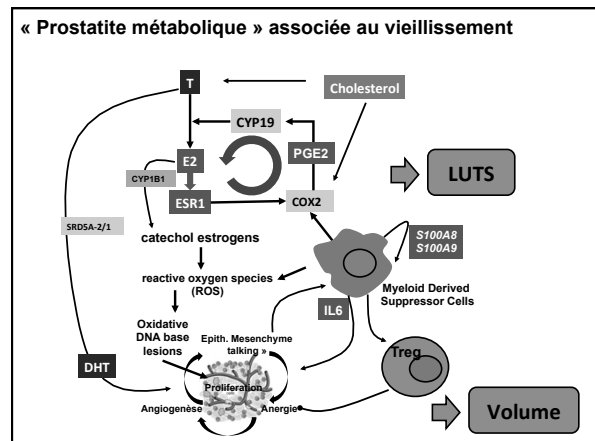
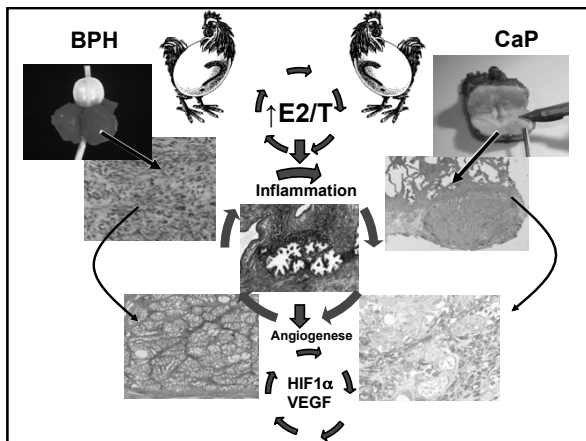
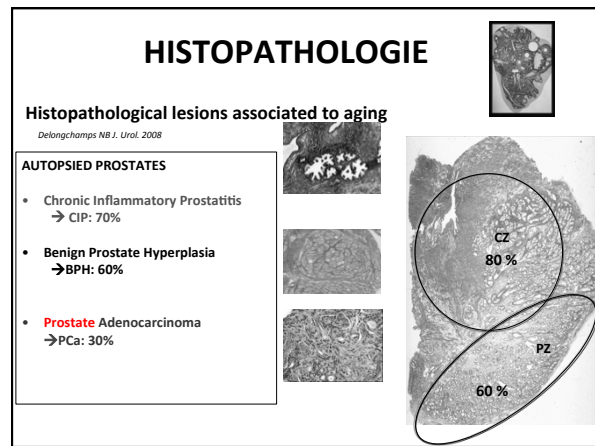
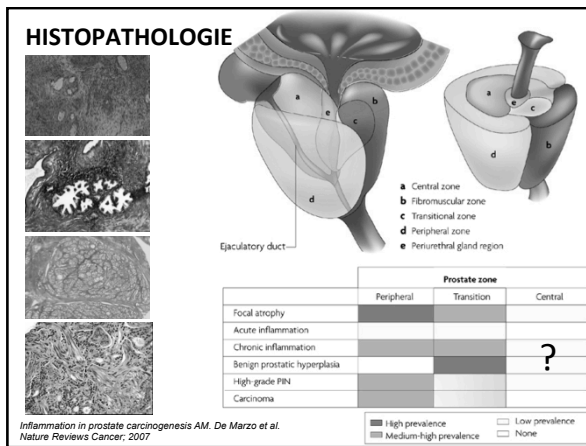
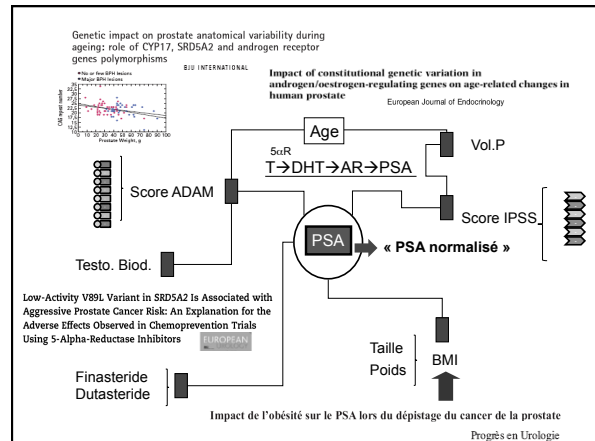
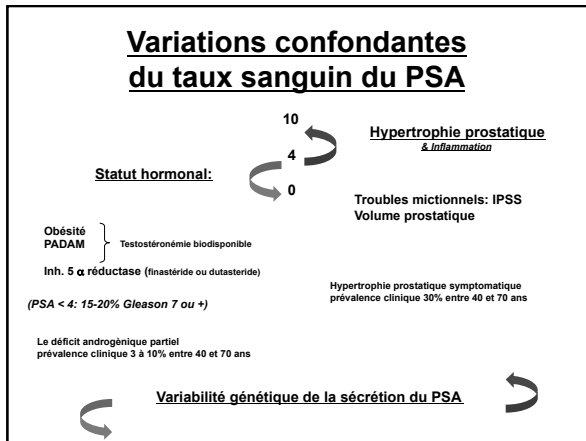
T+E → Vol. ↑, ADK

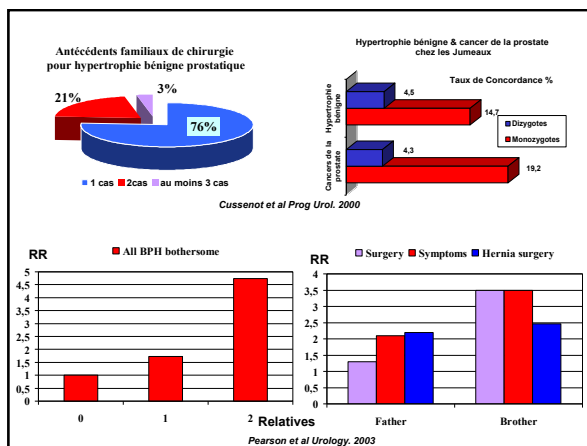
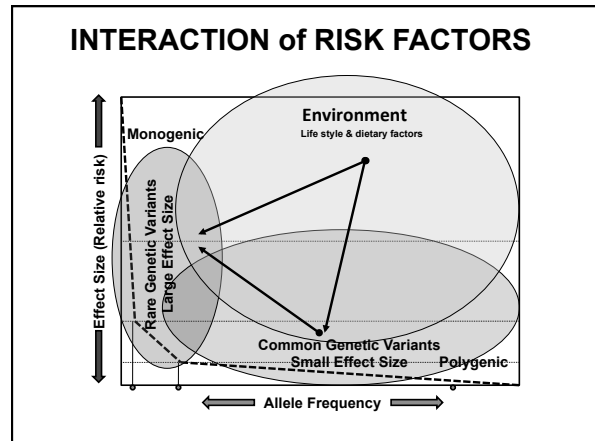
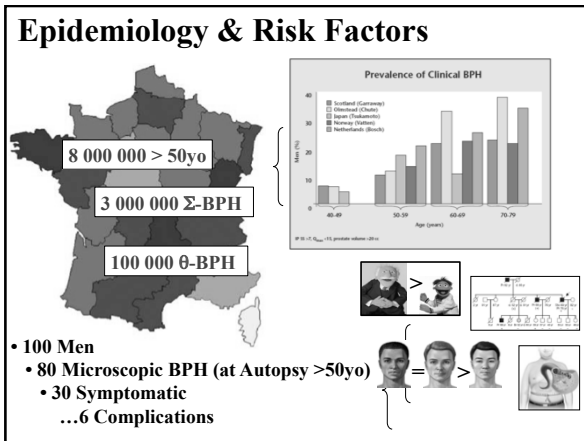
T → Vol. ↑, ADK

T+ (CYP19) → Vol. ↑ →









Caractéristiques histopathologiques des lésions d'hypertrophie bénignes dans les formes sporadiques et héréditaires

(d'après C.B. Doehring & al)

	Héréditaire	Sporadique
Age moyen (years)	59 +/- 3	70 +/- 7
Poids de la Prostate (g)	61 +/- 27	31 +/- 33
Ratio Stroma/Epithélium %	2.6 +/- 1.4	1.7 +/- 0.9

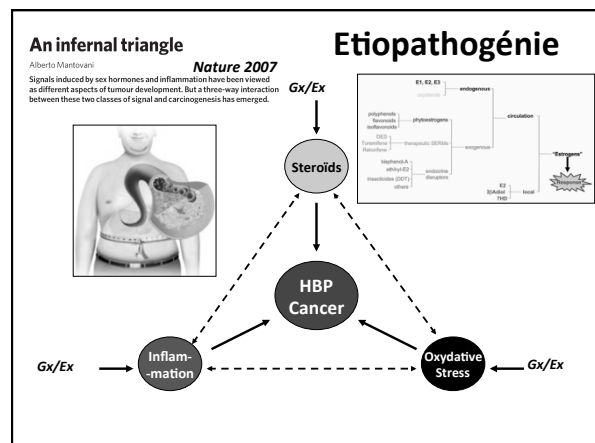
→ Quels sont les déterminants de l'hypertrophie?

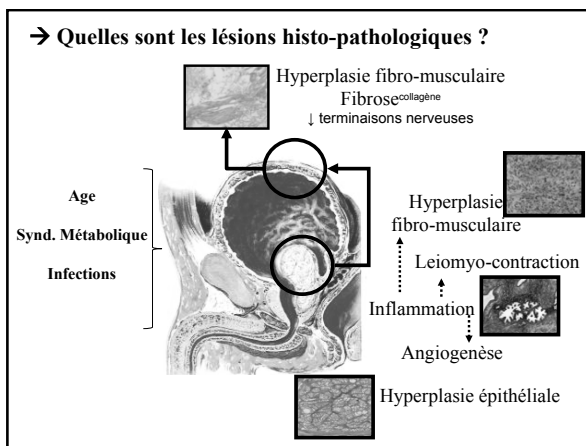
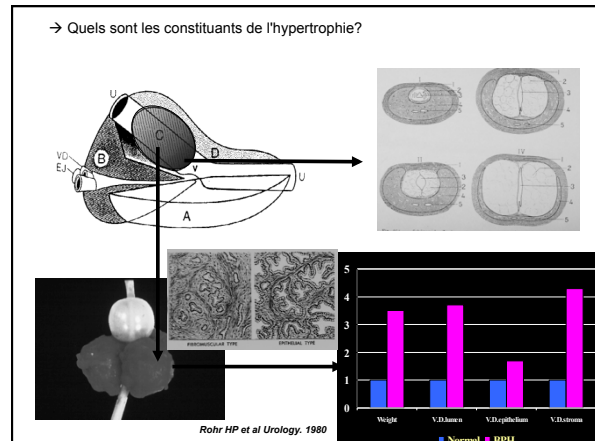
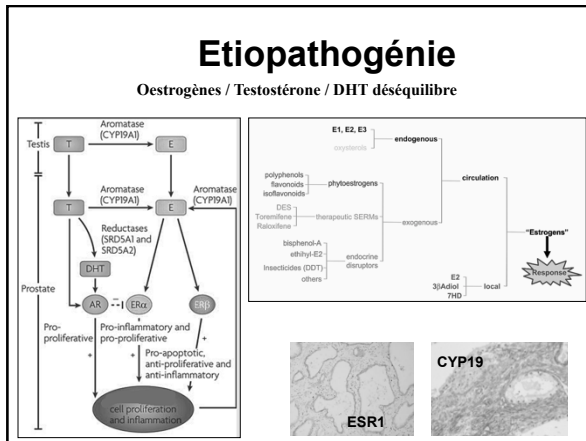
THEORIE "SYNCRETIQUE"

"Ageing disease"

Hypothèses

Oestrogènes / Testostérone / DHT déséquilibre
Stroma/ Epithelium interactions
Inflammation
cellules souches / réactivation embryonnaire

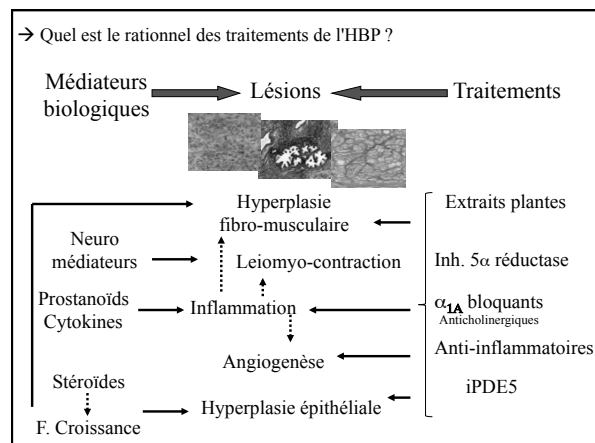
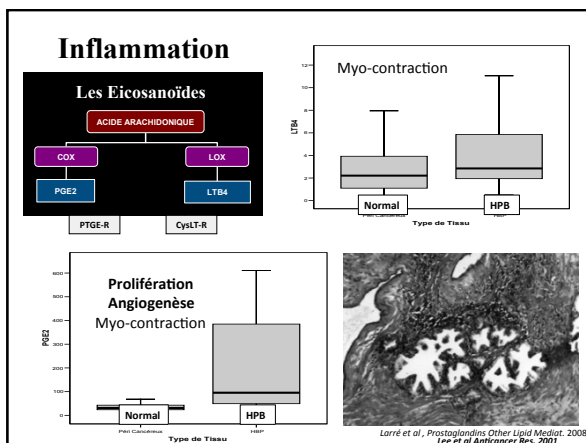


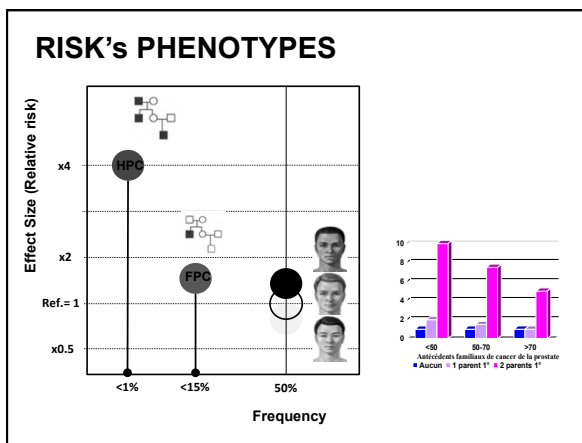
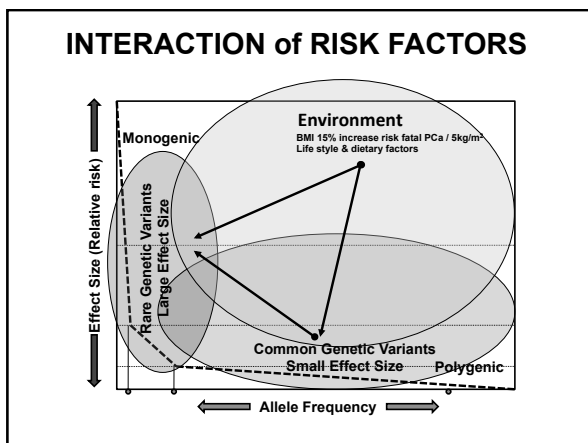
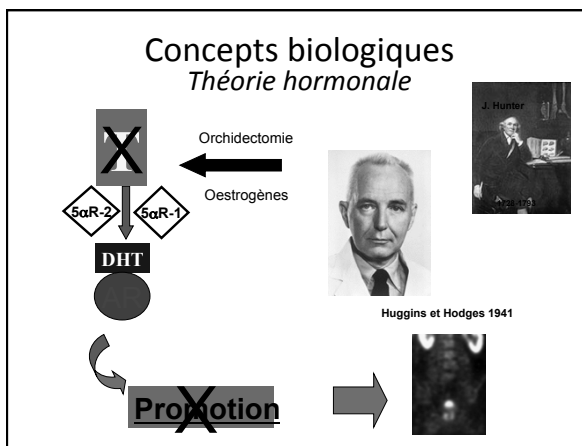
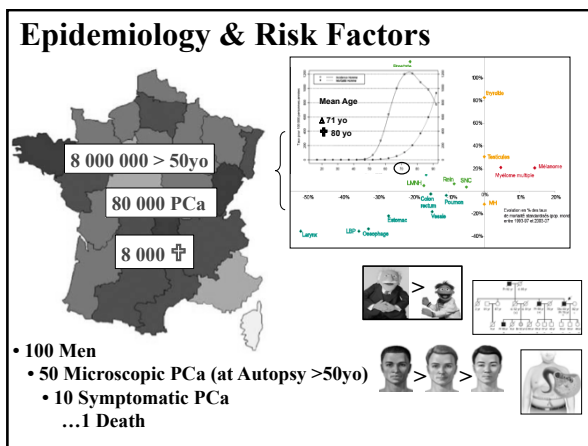
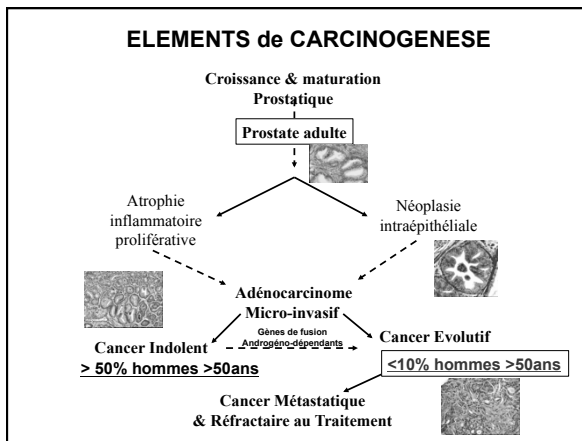
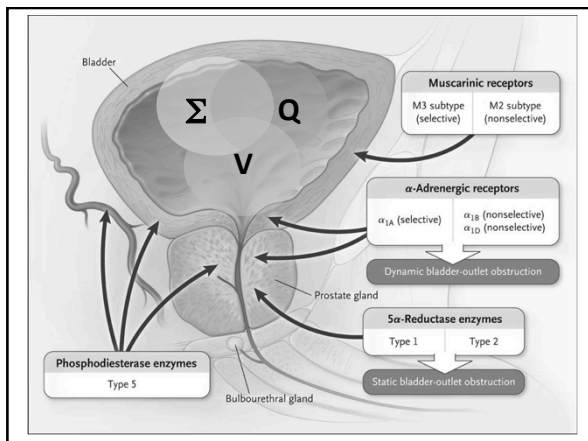


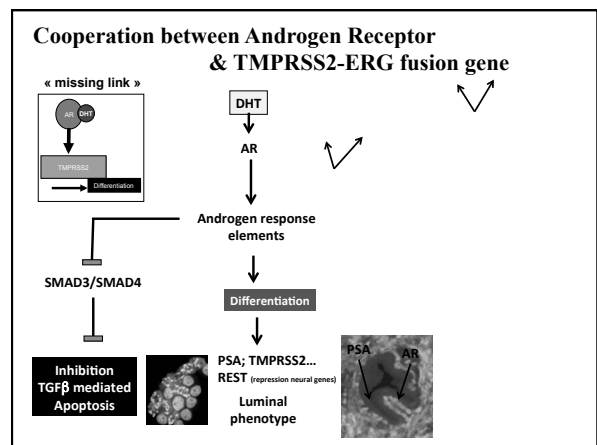
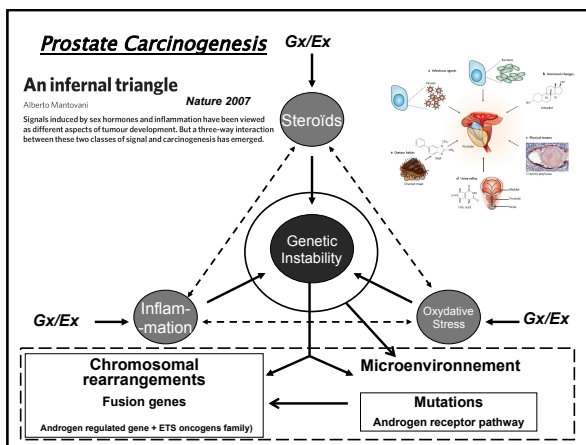
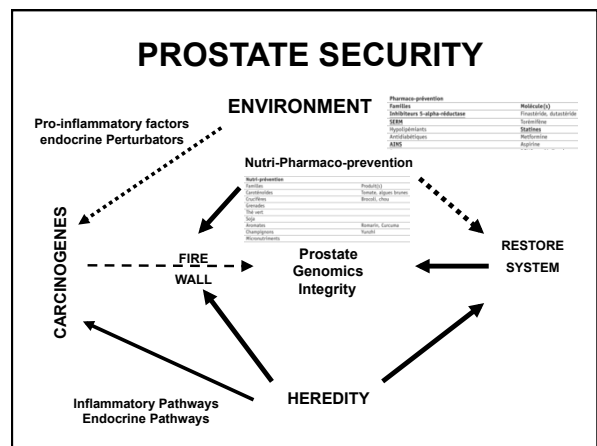
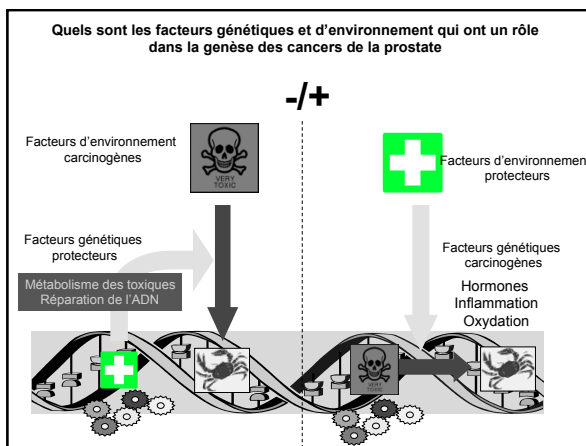
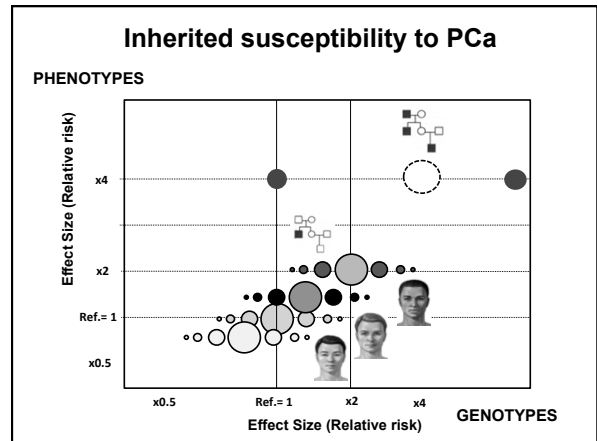
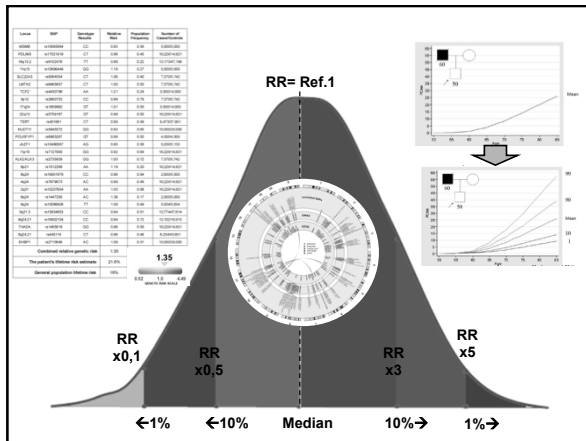
→ Modifications d'expression génique dans l'HBP

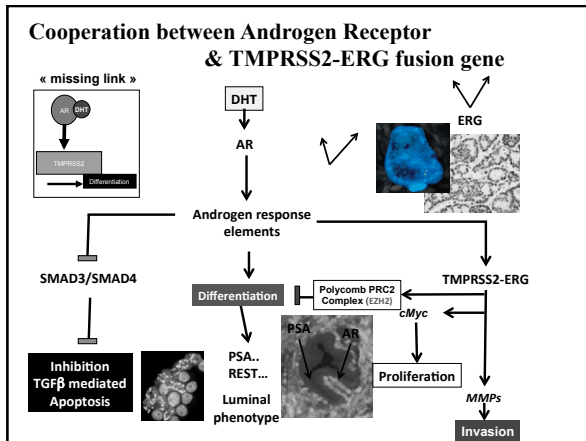
Gene	Description	Fold change	-60g BPH average	+60g
IGF2	insulin-like growth factor 2	21.02	19.89	22.16
KITLG	Kit ligand	15.46	15.27	15.65
FGF7	fibroblast growth factor 7	6.56	6.07	6.43
EGFR2100	epidermal growth factor receptor 2	5.88	5.71	6.61
ANGPT2	angiopoietin 2	4.88	4.88	6.27
HOX13	homeobox 13b	4.16	4.16	4.68
SLUG	neural crest transcription factor	4.16	4.16	4.62
ANGPT1	angiopoietin 1	4.16	4.16	4.83
PGR	progesterone receptor	4.00	2.95	5.05
KIS	kinase interacting stathmin	3.88	3.57	4.20
BMP4	bone morphogenetic protein 4	3.85	3.44	4.27
PPARG	peroxisome proliferator-activated receptor gamma	3.70	2.75	4.66
CXCL12	chemokine stromal cell derived factor 1	3.36	3.25	3.79
RLN	relaxin	3.36	2.51	4.21
EDNRB	endothelin receptor b	3.21	3.11	3.32
SPARC	osteonectin	3.10	2.76	3.44
PDGFRA	platelet derived growth factor receptor alpha	3.03	3.43	2.63
TIAM	T cell lymphoma invasion and metastasis	2.78	2.74	2.83
TM6SF2	transmembrane protein A15	2.75	2.50	3.01
KIT	C kit	2.72	2.70	2.74

Proton et al J Urol, 2004









Conception générale du traitement hormonal du cancer de la prostate

1- La prostate est un organe dont la croissance et la fonction sont sous la dépendance des androgènes. Les oestrogènes inhibent la croissance prostatique.

2- Le cancer de la prostate régresse sous traitement par privation androgénique ou par adjonction d'oestrogènes

Déductions logiques

- Traitement précoce, le + complet possible, continu et prolongé
- Prévention par déplétion androgénique possible
- Traitements substitutifs par les androgènes à déconseiller

