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PROSTATIC CANCER OF VIRAL ORIGIN: HOMOLOGY OF HUMAN ONCOGENIC PAPILLOMAVIRUS (HPV) L1 WITH NUCLEOPHOSMIN (NPM1), A CONTROLLER OF ANDROGEN RECEPTOR TRANSCRIPTION

Association de la Recherche contre les Tumeurs de la Prostate ARTP 2014, 19 November, Paris

Background: We showed previously that HPV contained **Prostatic Cancer (PC)** related oncogenic proteins:

1°) HPV **E2** (51-112) is homologous to an **Epidermal Growth Factor** (*Tran MKG, 1997*).

2°) **E1** to **PTEN**, **E6** and **L1** to the c-Myc inhibitor **Bin-1** (**B**ridging **i**ntegrator **1** or amphiphysin II), a tumor suppressor deleted in 42% of PC (*Tran GMK, 2008*).

3°) HPV-18 **E2** mimics **Osteoprotegerin** and **ParaTHormone** related **Protein** (PTHrP) active

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Saturday, 13 June 2015 11:07 - Last Updated Saturday, 13 June 2015 11:08

site (explaining bone metastasis). Anwar K (1992) found 80% HPV-18 in metastatic PC in Japan. Our meta-analysis concluded to a frequency of about 30%-40% (21-80%) oncogenic HPV (-16, -18, -33) in PC

(*EuroConf Cancer Pasteur Inst, 2004*).

The most important point is the

PCR (E6 primer and fresh tissue

); L1 primer and formalin-fixed, paraffin-embedded yielded negative results. For example, Terris MK (1997) obtained 21% positivity with E6 and 0% with L1 primer, in the

same

patients. Recent results confirm that use of paraffin-embedded tissues

(*Groom HCT, 2012; Ghasemian E, 2013*)

or L1 primer

(*Sylvestre RV, 2009*)

or both (13/104 versus 8/104

Aghakhani A, 2011)

were unsuccessful. Positive results were reported (in 10.5%

Jalilvand S, 2014;

worse overall survival,

Pascale M, 2013).

Noda S (1975) described **papillomavirus-like particles** in electron microscopy of prostate cancer tissue. Whitaker NJ (2013) found

koilocytes

in HPV-18 infected prostate cancer.

Our **aim** is to link HPV to Androgen Receptor (AR). Another hormonal cancer linked to virus is breast cancer, as the virus integration site is Aromatase, the estrogen synthetizing enzyme (*Tekmal RR, 1995*)

Methods: Amino Acid (AA) sequence comparison between HPV (*Lowe J, 2008*) and **NPM1 (nucleophosmin)**

, which controls

AR

transcriptional activity by promoting S-phase entry and hyperproliferation (cyclin switch D1 to E1 and p27kip1 loss)

(*Boudra R, ARTP 2013*)

. Clinically, high

p27kip1

is a correlate of better survival after prostatectomy at 5 years.

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Results: HPV L1 chimera (types 16, 18, 31, 33, 44, 56, 66, 115) [type-16, AA 167-219] is homologous to NPM1 chimera (human, duck, alligator, sheep, rhinoceros, turtle,...)[AA 1-48]

NPM1 MEDSMDMDSMQPLRPQMFLFGC- - - SGAHWARISPCSLGFFAGCELKSD

HPV L1 VEDSMDV – SMDPKQIQMFLI GCKPPTGEHWAR-SPCSPVG- --AGDCELKSD

Conclusion: Anti-androgen escape may be explained by AR mutations, but also in a PC subset (about perhaps 30%-40%, depending on the number of HPV serotypes screened) by a viral infection (oncogenic HPV), as HPV L1 is a viral NPM1 mimetic, enhancing AR transcriptional activity and inducing lethal p27kip1 loss. Japanese mushroom **Shii**

take

is a non toxic and highly efficient anti-HPV

(*Smith*

JA,

2014)

Indole 3 carbinol

from

cruciferous vegetables

(Brussels sprouts, broccoli)

are efficient against HPV-16 by viral transcription inhibition

(*Bradlow HL, 1999; Rieck GC, 2006*).

Anti-cancer drugs discovered by

HPV-18

infected KB cells screening

(*Perdue RE Jr, 1982*)

may act,

by

serenpidity

, as anti-HPV

: Taxol (Paclitaxel, Docetaxel, Cabazitaxel), topotecan, Vinca Alkaloids (Vinorelbine, Vinflunine)

HPV vaccination

of young men could protect against PC.

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