PROSTATIC CANCER AND HUMAN PAPILLOMAVIRUS (HPV): MOLECULAR HOMOLOGY OF HPV-18 E2 WITH ONCOGENE CRIPTO-1.

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BACKROUND HPV are found in Prostatic Cancer (PK) by PCR only when the primer is E (=Early) and not L (=Late) *(Tran GMK, 2004)*. This particularity may be explained by L loss during integration
(Johansson H, 2013)
. Cripto-1 (Teratocarcinoma-Derived Growth Factor-1), a member of Epidermal Growth Factor (EGF) family, is involved in PK progression
(Terry S, 2013, 2015)
. It is a co-receptor of TGF-β, induces E-Cadherin loss
(Zhong XY, 2008)
in Epithelial to Mesenchymal Transition
(Thiery JP, 2002)
and stimulates the PI3K/Akt pathway. E-Cadherin down regulation can also be induced by HPV E6

(Matthews K, 2003)
. As HPV contains many oncogenes implicated specifically in PK [HPV-11 E2 = EGF-HRG-TGFα mitogens chimera
(Tran MKG, 1997)
with a
common
M
H
I
E
S
L
hexapeptide, Osteoprotegerin in bone metastases
(Tran GMK, 2004)
, Nucleophosmin 1 (NPM1) in androgeno-regulation
(Tran GMK, 2014)
], we search for a molecular homology between Cripto-1 and HPV.

METHODS Amino acid sequences comparison of HPV with Cripto-1 EGF motif

CcxxGGxCxxxxxCxCxxxxxxxxC.

RESULTS

HPV-18 E2 113-**CF**k**KGG**q**TV** 45-**YF**d**GNK D** 127-**DGNKDNC**

Cripto-1 83-**CL**

HPV-18 E2 **96- W T L** **323-PPNN** **L** **KCWR**

Q
R
C
122-

V
Q
VYF

matches with Cripto-1 **120-D(W,T)L□□□□□ 124-LPKKcsLcKCWHgQIRC □□□1**
42 **-P**
Q
AFL

CONCLUSION The discovery of Cripto-1 being a viral HPV-18 E2 oncogene, whereas EGF is a HPV-11 E2, confirms the HPV role in PK, and E-cadherin loss as a factor of metastasis. A safe and efficient vaccine is warranted, as Gardasil and Gardasil 9 based on L1 may be followed by menopause/sterility and multiple sclerosis, and Cervarix by thrombocytopenia. A BT PHARMA vaccine based on a HPV-16 and -18 oncogene E7, instead of L1 as in Gardasil and Cervarix, is in phase II trial at the Pasteur Institute (Paris). E7 is much smaller than L1 and has less worrying epitopes.

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