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**C.86-Breast Cancer And Virus: Molecular Homology Between Human Mammary Tumor Virus 3'Orf And Scorpion Toxin, A Ligand Of Voltage-Gated Sodium Na<sup>+</sup> Channel. Omega 3, A Na<sup>+</sup> Channel Modifier, Reduces The Risk Of Metastatic Breast Cancer.**

Présentation Poster au 5<sup>o</sup> congress européen de virology (Lyon Septembre 2013) **REF 017 C**  
**ategory: 03.Innate immunity against viruses**

Breast cancer has multiple etiologies: Many virus were implicated [Epstein-Barr virus, Human oncogenic Papillomavirus, Adenovirus, Simian Virus 40 (SV40)]. Some discrepancies (Park DJ, 2011) can be relevant to this multiplicity of viruses. Other factors can be unrecognized: Genetics, radio-activity, aluminium, genetically modified organisms.

The human homologue of Mouse Mammary Tumor Virus (MMTV) (*Bittner JJ, 1936*), re-called

Human Mammary Tumor Virus (HMTV), was found in human Breast Cancer (BC), in variable % of cases: 74% in Tunisia, 42% in Australia, 38% in Italy, 36% in United States, 31% in Argentina, 0.8% in Vietnam (*Levine PH, 2004*).

This geographical disparity may depend on various factors, such as the degree of mouse infection by MMTV (*Stewart TH, 2000; Szabo S, 2005*).

The host susceptibility or resistance to MMTV is depending on the species genetic background, particularly the

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eceptor (TCR) Vbeta.

The MCF-7 and MDA-MB-231 breast cancer cell lines were demonstrated to be HTMV-positive  
(*Wang Y, 1995*);

when

injected in nude mice, they induce metastatic breast cancer  
(*Shafie SM, 1980; Price JE, 1990*).

In 123 treated breast cancers,

*Bougnoux P (1995)*

found after 48 months 70% metastasis if the breast fat alpha-linolenic acid (omega-3 precursor)  
level was low (9% if it was high): Thus, omega-3 (18:3n-3) protects against metastasis.

As omega-3 modifies the voltage-gated Na<sup>+</sup> channel (NaCh) (*Xiao YF, 2001; Banu I, 2006*), we  
looked for a NaCh ligand (scorpion toxin) in HMTV.

**METHODS:** Amino Acid (AA) sequence comparison.

**RESULTS:** we found a molecular homology between HMTV 3'orf and scorpion toxin chimera (*P  
ossani LD, 2000*)

/Euscorpis Flavicaudus (AAT76439) (58-71) implicated in development:

We demonstrated the HMTV oncogenicity by the discovery of 2 major oncogenes in the 3'ORF:

Mdm2, the p53 ligand (*Tran GMK, 2004*) and Notch-1 (*Tran GMK, 1998*). Furthermore, MMTV is a hormonal virus, because it integrated upstream of and activated Aromatase (Int-5), the estrogen synthetase (*T ekmal RR, 1997*)

## CONCLUSION

HTMV has 2 major oncogenes (mdm2, the p53 ligand, and Notch-1) and is a hormonal virus integrating upstream of and activating aromatase, the estrogen synthetase. HTMV 3'orf contains a scorpion toxin, explaining the metastasis protection conferred by omega-3, a NaCh blocker. The omega-3-rich soya diet in Asia, added to the low HTMV frequency in Asia (Japan, China, Vietnam), may explain the low asian breast cancer prevalence. We suggest to use omega-3 in association with chemotherapy in metastatic breast cancer; and study other second generation NaCh ligands (*Tran GMK, Allosteric EMBO Conf 2013; Djamgoz MBA, 2006*).

Green tea (*Yang CS, 2010*) associated with mushrooms were also very interesting alicaments (breast cancer risk reduction of 89%, with an odds ratio = 0,11 (*Zhang M, 2009*)). Corosol (graviola) was re-assessed: It down-regulates EGFR expression (

Dai Y, 2011

).

## BIBLIOGRAPHY

Banu I, Fraser SP, Djamgoz MBA. Docosahexaenoic acid (omega-3) blocks voltage-gated sodium channel activity and migration of MDA-MB-231 human breast cancer cells. *Int J Biochem Cell Biol*

2006, 38: 2173–82. Bittner JJ. Some possible side effects of nursing on the mammary tumor incidence in mice.

*Science*

. 1936, 84: 162. Bougnoux P, Lhuillery C. Acides gras polyinsaturés et cancérogénèse mammaire. In : Nutrition et cancer.

*CERIN Symposium, Paris,*

1995: 119-32. Dai Y, Hogan S, Schmelz EM et al. Selective Growth Inhibition of Human Breast Cancer Cells by Graviola Fruit Extract In Vitro and In Vivo Involving Downregulation of EGFR Expression.

*Nutrition Cancer*

2011, 63:795-801. Djamgoz MBA and Banu I. Dietary Compounds As Anti-cancer Agents: A Preliminary Evaluation of Ion Channels And Membrane Excitability As Possible Target Mechanisms.

*Turkish J Biochem*

2006, 31: 57–68. El Ayeub M, Darbon H, Bahraoui EM et al. Differential effects of defined chemical modifications on antigenic and pharmacological activities of scorpion alpha and beta toxins.

*Eur J Biochem*

. 1986, 155: 289-94. Kharrat R, Darbon H, Rochat H et al. Structure/activity relationships of scorpion alpha-toxins. Multiple residues contribute to the interaction with receptors.

*Eur J Biochem.*

1989, 181: 381-90. Levine PH, Pogo BG, Klouj A et al. Increasing evidence for a human breast carcinoma virus with geographic differences.

*Cancer*

. 2004, 101: 721-6. Park DJ, Southey MC, Giles GG, Hopper JL. No evidence of MMTV-like env sequences in specimens from the Australian Breast Cancer Family Study.

*Breast Cancer Res Treat.*

2011, 125: 229-35. Possani LD, Merino E, Corona M et al. Peptides and genes coding for scorpion toxins that affect ion-channels.

*Biochimie*

. 2000, 82: 861-8. Review. Price JE, Polyzos A, Zhang RD et al. Tumorigenicity and Metastasis of Human Breast Carcinoma Cell Lines in Nude Mice.

*Cancer Res*

1990, 50: 717-21. Shafie SM, Liotta LA. Formation of metastasis by human breast carcinoma

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cells (MCF-7) in nude mice.

*Cancer Lett.*

1980, 11: 81-7. Stewart TH, Sage RD, Stewart AF et al. Breast cancer incidence highest in the range of one species of house mouse, *Mus domesticus*.

*Br J Cancer*

. 2000, 82: 446–51. Szabo S, Haislip AM, Garry RF. Of mice, cats, and men: Is human breast cancer a zoonosis?

*Microsc Res Tech*

. 2005, 68: 197-208. Tekmal RR, Keshava N. Role of MMTV integration locus cellular genes in breast cancer.

*Front Biosci.*

1997, 2: d519-26. Tran MKG, Kirkiacharian S, Caprani A, Maurisson G. Molecular mimicry between HIV 1 Nef and human mdm2 ( mouse double minute 2), a ligand of p53, the major suppressor protein in oncology. XV Int AIDS Conf, Bangkok (Thailand), 2004: Abstr.

WePeA5599. Tran MKG, Kirkiacharian S. MMTV (Mouse Mammary Tumor Virus) 3'ORF mimicks the EGF family: EGF, Heregulin (c-Erb2 ligand), proto-oncogene Notch. Eurocancer 1998 (Boiron M, Marty M Ed). Paris, John Libbey Eurotext. p177 (P20).

[books.google.fr/books?isbn=2742002170](http://books.google.fr/books?isbn=2742002170).

Tran GMK, Caprani A. Voltage-gated sodium Na<sup>+</sup> channel allostery as the basis for the scorpion venom model of AIDS: Molecular homology between between spider toxin and HIV-2, and scorpion toxin and HIV-1 envelope gp41 sequence SWSNKS.

*Allostery EMBO Institut Pasteur*

*Conf*

2013, Sept 14-17, Paris. (On the site of : [Positifs.org](http://Positifs.org)). Wang Y, Holland JF, Bleiweiss IJ et al. Detection of mammary tumor virus env gene-like sequences in human breast cancer.

*Cancer Res.*

1995, 55: 5173-9. Xiao YF, Wright SN, Wang GK et al. Fatty acids suppress voltage-gated Na<sup>+</sup> currents in HEK293t cells transfected with the alpha-subunit of the human cardiac Na<sup>+</sup> channel.

*Proc Natl Acad Sci U S A*

. 1998, 9: 2680-5. Yang CS & Wang X . Green Tea and Cancer Prevention.

*Nutrition Cancer*

2010, 62: 931-7. Zhang M, Huang J, Xie X, Holman CD. Dietary intakes of mushrooms and green tea combine to reduce the risk of breast cancer in Chinese women.

*Int J Cancer.*

2009, 124: 1404-8. Acknowledgements: Association Positifs.

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