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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⁺ Channel. Omega 3, A Na⁺ Channel Modifier, Reduces The Risk Of Metastatic Breast Cancer.

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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⁺ 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 (*Zhan g M, 2009*)). Corosol (graviola) was re-assessed: It down-regulates EGFR expression (

Dai Y, 2011

).

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