There are no translations available.

Sydney, Australie, 22-25 juillet 2007

Dans la synthèse de cette Conférence, où notre association a vu trois de ses abstracts acceptés (un en Présentation Poster et deux autres en présentation CD), il a été présenté plusieurs milliers de communications, sans avancées majeures, si ce n'est l'élargissement de l'arsenal thérapeutique à de nouvelles molécules et classes de molécules. On peut par ailleurs regretter qu'il s'agisse du premier grand congrès international où toutes les approches alternatives ont totalement disparu. Enfin la distinction faite par le comité scientifique entre communications orales, poster et CD paraît plus guidée par l'intérêt des lobbies pharmaceutiques que par la qualité scientifique et l'intérêt des malades.

Nous évoquerons, successivement, la prévention, les traitements, puis les informations que nous considérons importantes dans le congrès off (posters et CD).

Préventions

Concernant la prévention, nous retrouvons comme dans les précédents congrès, en dehors du préservatif masculin et féminin, la circoncision et les microbicides.

Circoncision

La circoncision a donné lieu à une douzaine de communications qui ne font que confirmer le fort rôle protecteur de la circoncision dans la population hétérosexuelle. De plus, il ne semble pas que cette prévention désinhibe des pratiques à risques. Malheureusement, cette prévention reste trop peu utilisée, faute de campagne d'information efficace des autorités politiques. Concernant la population homosexuelle, il n'y a pas confirmation du rôle protecteur de la circoncision (étude australienne WEAC 103). Des études complémentaires sont nécessaires.

Microbicides

Pour les microbicides, les études réalisées conduisent à un optimisme modéré, les excipients ou adjuvants des molécules actives ayant souvent pour effet de provoquer une irritation ou une augmentation de la perméabilité de la muqueuse vaginale ou rectale. De nombreuses nouvelles molécules sont en cours d'essai. Un effort est fait sur la validation de l'efficacité sur la muqueuse rectale, non seulement dans l'intérêt

de la communauté homosexuelle, mais aussi hétérosexuelle, dans laquelle une forte minorité pratique la sodomie. Enfin il a été montré que les lavements avant la sodomie, ainsi que l'utilisation de gels lubrifiants non iso-osmotiques, fragilisent la paroi rectale en la rendant plus perméable et augmentent le risque de transmission du HIV.

Recherche clinique

L'essentiel des communications en recherche clinique a porté sur de nombreux essais avec de nouvelles molécules. Cette recherche est motivée par l'existence d'une minorité (5-10%) de patients résistants à tous les antiviraux du marché, mais aussi par la volonté des firmes pharmaceutiques d'augmenter leur part de marché avec des molécules plus efficaces, plus onéreuses et présentant moins de résistance et d'effets indésirables. Rappelons que Positifs ne soutient pas cette orientation pour répondre à l'échec thérapeutique. En effet, depuis 1989 « Positifs » défend et rappelle à chaque congrès, sans être entendu, l'intérêt de la tacrine comme antiviral (action anti-reverse transcriptase), sur la base d'essais cliniques publiés. De plus « Positifs » a établi et publié dans divers congrès que la tacrine agissait via un canal ionique de la membrane cellulaire, récepteur qui restait par conséquent insensible aux mutations du virus. L'utilisation de ce seul antiviral efficace, dont la légère toxicité hépatique peut être compensée par le chardon Marie (Legalon), aurait pu éviter l'hécatombe d'avant 1996 (arrivée des trithérapies), permettre de traiter à faible coût les patients des pays en voie de développement, éviter la course effrénée à de nouveaux antiviraux, et concentrer les moyens à la recherche fondamentale et à la fabrication d'un vaccin

Parmi les nouveaux antiviraux les plus prometteurs citons :

- une antiprotéase, le darunavir, qui, boosté par le ritonavir, est plus efficace que le Kalétra sur un essai de 48 semaines en monothérapie
- une anti-intégrase, le raltegravir, qui dans une association avec tenofovir, lamivudine, donne sur une durée de 48 semaines des résultats comparables à ceux de l'Efavirenz
- un inhibiteur de fusion (Poster MOPDX01), non peptidique, biodisponible oralement, de faible poids moléculaire (470), qui pourrait être une alternative à l'enfuvirtide, d'utilisation difficile (injection sous-cutanée journalière, avec effets indésirables). Ce composé, contrairement à l'enfuvirtide, se fixe directement sur l'enveloppe du virus dans la première étape et non sur le recepteur CD4.
- un anti CCR5, le INCB009471, qui possède une très puissante et rapide action antivirale sur un essai de 15 jours en monothérapie.

Indiquons un essai clinique sur un autre anti-CCR5 (Abstract TUAB 102), le vicrivoc, sur 118 patients, en double aveugle contre placebo, sur une durée de 48 semaines. Même s'il présente une bonne activité antivirale, nous ne pouvons que le déconseiller aux patients. En effet, plus de 10% des patients traités (7/60) présentent une pathologie tumorale au cours de l'étude. Même si les auteurs qui, pour sauver leur produit, indiquent pour le groupe placebo un taux comparable de pathologies tumorales (2/28), il existe manifestement un biais lié à la faible taille du groupe placebo ou un faux délibéré. Nous ne pouvons que rappeler et constater que dans l'ensemble des grands essais cliniques sérieux publiés, le taux de pathologies tumorales ne dépasse pas 3% !

Au niveau du vaccins tant prophylactique que thérapeutique, constat d'échec. Nécessité de coordonner tous les efforts et de développer la recherche fondamentale.

Enfin, concernant la stratégie de traitement intermittent programmé, que les lobbies avaient enterré avec l'essai SMART, une seule étude (TUPEB 038) montre qu'il n'y a pas de risque d'échec thérapeutique à la reprise du traitement, indépendamment de l'apparition possible de mutation pendant l'arrêt.

Le Congrès off

Concernant les informations intéressantes du congrès off que nous souhaitons diffuser, nous citerons :

L'utilisation du Coenzyme Q10(déjà bien connu des patients ouverts aux traitements alternatifs) dans le traitement des neuropathies périphériques induites par les NRTI (d4T et ddI). Rappelons que la L-carnitine (Levocarnil) est également utilisée pour ce type d'effet indésirable.

En résumé, en dépit de l'acharnement des lobbies pharmaceutiques à enterrer les traitements par intermittence avec l'essai SMART qui a gaspillé un budget considérable au détriment d'une recherche clinique utile au patient, toutes les études convergent pour montrer le bien-fondé de cette stratégie thérapeutique, même si des études restent à faire pour établir les critères de sélection des patients pouvant bénéficier des plus longues interruptions.

Le mannose pourrait peut-être constituer le traitement idéal du HIV, sans aucun effet indésirable et sans résistance (action sur un récepteur cellulaire). En effet, deux

communications Poster (WEPEA 011 et WEPEA 016), montrent que le récepteur au mannose constitue un co-récepteur du HIV. Or, rappelons qu'une communication Poster au 14° ISHEID à Toulon en 2006 avait présenté un cas clinique d'un couple sérodiscordant chez qui l'homme séronégatif ne possédait pas de récepteurs au mannose. Il semblerait donc que le récepteur au mannose soit nécessaire à l'infection et que la saturation de ce récepteur par du mannose à des concentrations (de l'ordre de 50mM) empêche l'adhésion du virus à la membrane cellulaire. Partant de ces résultats, « POSITIFS », envisage de proposer un protocole d'essai clinique chez des séropositifs naïfs ou traités avec une charge virale détectable, pour lesquels la charge virale sera suivie en fonction de la supplémentation en mannose. Rappelons que le mannose est un sucre naturel contenu dans certains végétaux de notre alimentation (choux, pomme de terre, notamment), à des doses trop faibles pour avoir une activité anti HIV, et qu'une supplémentation à forte dose, nécessaire à une activité antivirale potentielle, ne provoque aucun effet indésirable, diabète entre autres.

Contribution de POSITIFS

À partir de recherches fondamentales en mimétisme moléculaire, POSITIFS ouvre de nouvelles voies de traitement pour la sclérose en plaques (utilisation d'anti herpès), l'athérosclérose avec un vaccin contre un virus aviaire, le virus de Marek (qui devrait être recherché systématiquement chez tout séropositif présentant une athérosclérose), la tuberculose avec un vaccin.

Communication MOPE A012

Multiple sclerosis and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP): Molecular mimicry between
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irus (MSRV) gag capside at the triproline motif.

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Human T-cell leukaemia virus 1 (HTLV-**1**) infection is endemic in well-defined geographic regions, and it is estimated that some 20 million individuals are infected worldwide. HTLV-1 is a retrovirus aetiologically associated with
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ymphoma/leukaemia (ATL), mycosis fungoides, interstitial pneumonitis, a subset of rheumatoid arthritis (Zucker-Franklin D., 2002) and Sjögren's syndrome (sicca syndrome) in humans. Most infected individuals are asymptomatic carriers; only 2 to 5% will develop a chronic encephalomyelopathy,
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araparesis (HAM/TSP) (Beby-Defaux A., 1999). Recently, the second type (HTLV-2) has been found in TSP among Amerindians, with a periventricular demyelinisation (Beilke M.A., 2005 ; Araujo A., 2004). HAM/TSP possibly mimics multiple sclerosis (MS) (Koprowski H.). Three viruses at least were found in MS: Epstein Barr virus, HHV-6 (Challoner) and MSRV (Perron H.).

OBJECTIVE: To link demyelinisation in MS and HAM/TSP to these viruses. METHOD: We compared amino acid sequences of MBP, HTLV-1,-2, HHV-6 and MSRV.

RESULTS : There is a perfect molecular mimicry in a heptapeptide P**RT**PPP**S** between HHV-6 U24 and MBP that permitted to center the alignment :

MBP shark	**KK**	**GKG**			
MBP human	**VT**	P	**RT**	PPP	**S**
HHV-6 U24	P	**RT**	PPP	**S**	
MSRV Gag	**S**	P	**QS**	PPP	
HTLV-2 Gag-15	**VQ**	P	**RR**	PPP	**Q**
HTLV-1 Gag-15	**VQ**	P	**KK**	PPP	**N**

CONCLUSION: The demyelinisation observed in HAM/PST and MS is explained by a molecular mimicry between myelin MBP and the 4 viruses found in these neurologic diseases: HTLV-1, -2 for HAM/TSP, HHV-6 and MSRV for MS; this is a molecular confirmation of virologic findings which reinforce and complete virus isolations. This epitope is restricted by HLA DR15; it is logical to treat HAM/TSP and MS with antivirals specific of retrovirus and herpes virus.

Poster MOPE A012

MULTIPLE SCLEROSIS: MOLECULAR MIMICRY BETWEEN THE BASIC PROTEIN OF THE MYELINE, HTLV-1, -2Gag p15, THE HUMAN HERPES VIRUS-6 AND RETROVIRUS MSRV (GAG, CAPSID): EPITOPE RESTRICTED BY AND INDUCING AN EXPERIMENTAL ENCEPHALOMYELITIS IN THE MOUSE

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BACKGROUND

The multiple sclerosis (MS) is a clinically heterogeneous auto-immune disease: Many clinicians think that there is not one, but several MSs, gathered under the same term. It is a rigid clinical framework to dismember, with the modern means we currently have. Right now, it seems that one can distinguish approximately 5 different varieties, as suggested by the histological studies (STORCH M and LASSMANN H, 1997). Antigen HLA-DR2 is overrepresented in this disease; in particular, in the multiplexing families where this antigen is expressed, the risk to contract a SEP is up to 40 to 50 times higher than for a normal population. Paradoxically, the studies among twins monozygotes show only one agreement of 25-30%, i.e. of the same order as for the poliomyelitis, a viral disease; what suggests a prevalent environmental cause, in 70-75% of the cases, in the SEP. Two viruses were implied in the SEP: The Virus Human Herpes 6 (VHH-6) (CHALLONER PB, 1995) and the retrovirus of SEP (MSRV= Multiple Sclerosis Retrovirus) described by Herve PERRON. MULTIPLE SCLEROSIS AND VIRUS HERPES HUMAIN-6 (VHH-6). With regard to the VHH-6 (re-examined in: CAMPADELLI-FIUME G, 1999), virus ubiquitaire responsible for the infantile roseola (exanthème sudden or 6th disease) and for 26% of the feverish convulsions of the child, it was described an acute fulminant demyelinisation due to the VHH-6 at a subject not immunodéprimé. Rejections of Clerc's Offices and deaths by encéphalite are observed among persons receiving a transplant (DROBYSKI WR, 1994; BOSI A, 1998). Of IgM against the HHV-6 were found in the event of chronic syndrome of tiredness, which is to be brought closer the tiredness frequently observed in the SEP (tiredness, although nonspecific symptom, is a true handicap specific to the SEP). In the same way, the HHV-6 was blamed in a retinite at a sidéen (QAVI HB, 1989), recalling in this direction the optical neuritis so evocative of the SEP. The HHV-6 can be responsible for hepatitis (TAJIRI H, 1990), even of fulminant hepatitis mortal (ASANO Y, 1990). Generally, the VHH-6 is regarded as a virus ubiquitaire, contracted during the first 2 years of the life, which is in agreement with the epidemiologic data on the SEP of the migrants, though the serologic studies show that the VHH-6 is less frequent in France (approximately 30% of seropositivity) and in Great Britain (~ 40%) that in the United States (~90%). The tables of encéphalite serious are seen especially in the event of immunodépression (AIDS and persons receiving a transplant). Among persons receiving a transplant, the HHV-6 is associated the rejection of Clerc's Offices (AGUT H, 1991). How to explain that a virus as ubiquitaire as the HHV-6 can be in question in the SEP? One can suppose that occurred of a SEP is due to the meeting of a factor of risk like the antigen of susceptibility HLA-DR2 and one or more virus. [An example is that of the virus of measles which is extremely banal, but can in rare cases entrainer an acute encephalitis or a Subacute Sclerosing Panencephalitis (PESS) extremely serious]. Of another factors, like the female sex, where antigens HLA are expressed than at the man, can intervene: It is known for example that the autoimmune diseases, generally, have a greater predilection for the women. The genetic study of the SEP showed several candidates, of rather moderate effect (what corresponds well to the concept of factor of risk, associated an environmental factor), rather than a single major gene for important purpose: The SEP is not a monogenic disease. Certain genes are found by several independent teams. One can quote of course antigen HLA-DR15 and/or HLA-DR4 (chromosome 6q), certain patients reached of SEP which can have the 2 HLA-DR (HLA-DR15 and HLA-DR4), but also another area close to HLA in the 6q (on this subject, it is interesting to note that the MOG is located at the level of the 6q). For the moment,

certain genes seem to have a moderated effect, but they ask to be confirmed in a final way by other teams: The PBM of the myelin itself, but only in one Finnish population well defined geographically, the receiver of), the chains door of immunoglobulin, the IL-2, the Protein Kinase C-delta (PKC- T-Cell Receptor (TC R).

*Nota Bene foot-note: The nomenclature of antigens HLA is enough changing, with the result that the same antigen is called differently according to whether the article is recent or old: HLA-DR2 is the old denomination of HLA-DR15, which itself is dethroned by most modern but more complicated nomenclature HLA-DRB1*1501. Antigens HLA were the subject of a recent development (KLEIN J and SATO A, 2000). The genes of class II are indicated with 3 letters: 1st (D) indicates the class, the 2nd (M, O, P, Q, or R, respectively). HLA-DRB, for b or a family, and 3rd (A or B) the chains. The b example, means gene of class II of the family R coding for the chains individual genes of system HLA are differentiated by Arab numbers, and the notation for many the variable alleliques ones of these genes is a number preceded by an asterisk (*). For example, HLA-DRB*1501 wants to say varying allelic 1501 of the gene 1, which codes molecule of class II b pertaining to family R.*

A recent Australian study seems to show that all is played on level of a simple residue, a Valin (Valley or V) located at the level of antigen HLA-DR: In this direction, it is more important to have this Valin than to have antigen HLA-DR15. I.e. even without having antigen HLA-DR15, one can make a SEP, since one has this crucial Valin. The smoothness of the epitopic recognition is thus extreme, and it would be from now on necessary to resort to a detailed and targeted sequencing, in the search of this valin, to identify antigen HLA-DR (Valley) of susceptibility to the SEP. It is interesting to note that the VHH-6 can transactiver a retrovirus, if one remembers that the MSRV is a retrovirus (RV=RetroVirus). The decisive study implying the VHH-6 in the SEP is that of CHALLONER PB into 1995 which in found in the plates of demyelinisation of the SEP, on the level of the oligodendrocytes, the cells which synthesize the myelin central nervous system, but also on the level of the neurons; it used a method of immunocytochemistry with an anti-101K antibody (gp110) of the VHH-6. [We underline this detail, because we found that the 101K has a sequence (QYLKSK) which is almost identical to that of the bovine 1 human A an anti-VHH-6 activity in vitro on b2 (EYLKSK); interferon-b interferon-blood cord cells (FOLGER K, 1995) and is a drug authorized in the SEP, able in the very early forms, as of the first sign, to decrease by 44% the risk of occurred of a clinically definite SEP (JACOBS LD, 2000)]. SOLDAN SS and BERTI R (1997) detect by PCR (Polymerase Chain Reaction) brood, method more significant than the simple PCR, of the HHV-6 in ~ 40% of SEP. It of IgM, and not of IgG, is directed against early protein p38/41 of the HHV-6, which is present in the SEP, testifying that it is about a reactivation of the virus. Very many authors launched out recently in the research of the VHH-6 in the SEP: In short, one can say that they confirm, for the majority, the role of the VHH-6 (failures being able to be explained by a technique different, less significant, and/or the heterogeneity of the SEP): One can quote ABLASHI FD (1998) which finds in 56¨% of SEP of IgM against the early antigen p41/38, ONGRADI J (1999) in 44% of SEP of IgM against variable the 6B of the VHH-6, KIM JS (2000)

in 20,6% (7/34) of SEP by PCR brood. MULTIPLE SCLEROSIS AND RETROVIRUS MSRV Of HERVE PERRON. With regard to retrovirus MSRV, one notices first of all that other retroviruses were implied in the models of SEP: Visna-CAEV (Caprine Arthritis Encephalitis Virus), a lentivirus of the goat and sheep which has a sequence resembling myelin; Human T Leukemia Virus HTLV-I (but also HTLV-II), person in charge for tropical spastic paraplegia and the myelopathy associated with the HTLV in a very small percentage with case, after a very long latency period, and whose protein gag presents the very interesting sequence with a triplet of prolines (Pro or P) "PPP". On this subject, KOPROSKI H had found antibodies anti-gag of HTLV-I (due to a cross reactivity) in the SEP, and this work had initiated research on the specific retrovirus of the SEP, whose result is the discovery by Herve PERRON of the MSRV in ~ 30% of the SEP. We were also binterested in the retrovirus, and found (TRAN MKG, 1999) a dream of interferon- of mouse in the gp41 of the VIH1. There still, in the context of the SEP, one, as in the case of the protein-b falls down very curiously on the interferon-2 (TRAN MKG, 2000). b101K of VHH-6, which is very homologous with the interferon-b.

OTHER VIRUS AND MULTIPLE SCLEROSIS. The other viruses are, in terms of frequency, less important, and work with regard to them is less advanced. The candidates are extremely many, most interesting are perhaps: The virus of the disease of Square, or Canine Distemper Virus (COOK), of the same family as the virus of measles, the virus herpes simplex (GAUTAM), [only one publication gives a report on SEP associated with the virus herpes], Coronavirus, of the family of the virus of hepatitis at the mouse (Murine Hepatitis Virus or MHV) and the virus of EPSTEIN-BARR. The virus herpes of the monkey squirrel SAIMIRI (GAUTAM) contains a homologous sequence with final part NH2 of the PBM; when it is injected with complete additive of Freund, it causes an experimental allergic encephalomyelitis in the mouse (whereas if it is mixed with the incomplete additive, it is protective). We studied this viral sequence more thoroughly, by extending the bank of data and by indexing all the sequences published of the species of myelin, and we are seen that it was homologous with the ox myelin, species not analyzed by GAUTAM. Consequently, there is the typical example of a molecular mimicry between a virus of the herpes family, like the HHV-6, and the PBM, on the level of the NH2 terminus of the myelin. This short viral encephalitogene is restricted by the TCR Vb in the SEP. This data join the b peptide studies of genetics on the possible role of the TCR Vb, and also the only and single publication on the implication of a virus herpes simplex in the SEP. Although anecdotic, this study has the merit to highlight the molecular mimicry between the herpes virus family and the myelin.

OBJECTIVE

We seek to show the viral origin of the SEP, because an antiviral treatment, available, against the VHH-6 [to ganciclovir, and its bioavailable version to valganciclovir it (Laboratories ROCK), whose advantage is to be usable by oral way, foscarnet for example (AGUT H, 1989)], or an antiretroviral like those used in AIDS, could be used to treat this disease.

In the same way a vaccine against the SEP could be considered.

METHOD

The comparison of the sequences in amino acids of proteins and that of the corresponding nucleotidic sequences. The Basic Protein encephalitogene of Myeline (PBM) and viruses are analyzed HHV-6 (variable a: U 1102, variable b: Z29 & HST) and MSRV. The choice was made on the PBM because it induces in the animal an experimental allergic encephalomyelitis (EAE). In particular, in mouse B10.RIII (H-2r), the épitope 89-101 of the PBM 89VHFFKNIVTPRTP101 causes a serious EAE, at early beginning, of evolution chronic and repeating (JANSSON L, 1991). We also centered research on the peptide of the PBM restricted by antigen HLA-DR15, a sub-type of HLA-DR2 (MARTIN R, 1991), which is overexpressed by the patients reached of SEP. It is that this peptide 91-102 of the PBM has as a sequence "91FKNIVTPRTPPP102", i.e. it covers the same area as the peptide of JANSSON. The statistical analysis is made according to OLDSTONE MBA, which assumes that there are 20 Amino Acids (AA), that each one among is balanced same unit coefficient 1.

Therefore, for example, if the molecular mimicry relates to 6 successive identical residues, there is 1 chance out of 20 power 6 (206 = 20x20x20x20x20x20 = 64.000.000) so that it is due to the simple chance, according to the law of the great numbers. A molecular mimicry is statistically significant starting from the size of the hexapeptide (6 AA, 6 acids amino). The abbréviations employed in peptidology are: With = Ala, Alanine; B = Asn or Asp, Asparagine or Acid Aspartic; C = Cys or Cysteine; D = Asp or Acid Aspartic; E = Lime or Acid Glutamic; F = Phe or Phenylalanine; G = Gly or Glycine; H = His or Histidine; I = Iso or Isoleucine; K = Lily or Lysin; L = Leu or Leucine; M = Met or Methionine; NR = Asn or Asparagine; P = Pro or Proline; Q = Gln or Glutamine; R = Arg or Arginine; S = Ser or Serine; T = Thr or Thréonine; V = Valley or Valin; W = Trp or Tryptophan; X = unknown; Y = Tyr or Tyrosin; Z = Gln or Lime, Glutamine or Acid Glutamic.

(For the biologist, sequence PRTPPPS can be also written: Pro-Arg-Thr-Pro-Pro-pro-Ser, and means: Proline-Arginine-Thréonine-Proline-Proline-Proline-serine).

RESULT

There exists a perfect molecular mimicry between the PBM, precisely on the level of this peptide PRTPPPS, and the protein U24 (U = Unique) of VHH-6. This mimicry extends over a length from 7 consecutive residues, which is very highly significant: There is 1

chance out of 20 power 7 (207 = 1.280.000 000) so that it is a simple coincidence. Downstream, there is a common RPWN sequence. Upstream, there is IFVV (~the VVHFF opposite).

Virus the 3 VHH-6 (U24) VV IFK. PRTPPPS... ...RPAWN (U1102 stock) Myelin PBM (exon 3-4) VVHFFK. PRTPPPS... ...RP - WN (PBM intron 4-5)

On the nucleotidic level, one finds a homology of 19/22 identical bases (86,4%), of which a perfect imitation on 11 consecutive bases.

HHV-6 (U24) DC cct cgg acg ccg ccg ccg human Tc
PBM DC ccg cgt acc ccg ccg ccg Tc (KALMHOLZ J, 1986; NYE HS, 1995)

The MSRV (gag, capsid) is also very homologous on the level with the triplet of prolines PPP:

Virus	MSRV (gag, capsid)	PYVQTFF	S
Virus	VHH-6 (U24)	**VV IF**	K PI
Myelin	PBM (exon 3-4) (man)	PVVHFFKNIVTPRTPPPS	
Myelin	PBM (exon 3-4) (bird)		S
Myelin	PBM causing an EAE	VHFFKNIVTPRTP	
Myelin	PBM restricted by HLA-DR15	FKNIVTPRTPPP	

Like negative control, one can note that the VHH-7, which was never found in SEP, by any author, despite all studies which were made (ONGRADI J, 1999), has on this level (U24) sequence 1 MTHETPPPS 9 (MEGAW AG, 1998; NICHOLAS J, 1995), which one notes that it does not have a basic arginin (Arg or R), but has an acidic Glutamic Acid residue (Lime or E).

However in the PBM of the myelin, the arginin is essential, because it belongs to a motif for RTP phosphorylation (Arg-Thr-Pro), which is preserved in VHH-6, but not in U24 of VHH-7 which has ETP (Lime-Thr-Pro).

The sequence of U24 of VHH-7 is thus very different functionally, i.e. it cannot be

phosphorylated, although there is a little similitude, of purely phylogenetic nature with VHH-6 (associated with species evolution, without any medical consequence).

VHH-7 seems to be implied in a skin trouble, the pink pytiriasis. In the same way the VHH-8, isolated in patient with Kaposi sarcoma, but never among patients with SEP, does not have this sequence either. One sees here the power of the molecular mimicry like methodological approach, because one cannot force negative controls to be mimetic to myelin.

The phosphorylation is carried out by a serine/threonin kinase activated by the meiosis of 44kDa (p44mpk) on the threonin (Thr) residue T 97 of reason RTP (Arg-Thr-Pro) of the sequence 91 NIVTPRTPPPSQGK 104 of the bovine myelin (SANGHERA JS, 1990).

CONCLUSION

There exists a molecular mimicry between basic protein encephalitogene of the myelin and the virus human-6 herpes (U24) and a strong homology with retrovirus MSRV (gag, capsid). HHV-6 and MSRV are the 2 viruses implied in the multiple sclerosis. The common area is also that restricted by antigen HLA-DR15 (a sub-type of HLA-DR2) overexpressed in the SEP; its injection in the animal having the antigen suitable H2 causes an experimental allergic encephalitis. We confirm work of CHALLONER PB and of many authors on the role of HHV-6, like those of Herve PERRON on the MSRV, by unifying them on same the epitope of MBP. Vaccine and antiviral drugs are possible in the SEP.

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Communication CD A006

Atherosclerosis and AIDS: Homology between avian Marek's herpes virus and Low Density Lipoprotein cholesterol receptor (LDLR).

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Context: HIV-1 infected patients are very susceptible to herpes virus family infections (herpes simplex 1 and 2, cytomegalovirus, chickenpox zoster virus, HHV-6, Epstein-Barr virus, HHV-8), the last 2 inducing also lymphomas. We studied avian [an avian virus can infect humans, i.e. influenza virus] herpes Marek's virus, which causes in poultry either atherosclerosis (coronary, aortic, mesenteric) even with a diet without cholesterol, or lymphoma. Cholesterol crystals were found in cell cultures infected by feline herpes virus.

Objective: To study Marek's virus mechanism of action in atherosclerosis.

Methods: Amino acid (aa) sequences and three dimensional (3D) structure comparison. Results: Marek's virus contains a 132 base pair (bp) (~ 42 aa) repeat (sometimes in 8 copies), which is homologous to the 8 repeats of 42 aa in the LDLR (LDLR is mutated in familial hypercholesterolemia and in Watanabe rabbit, an atherosclerosis model) and the macrophagic scavenger receptor, implicated in cholesterol arterial deposition:

Marek's virus repeat

LDLR repeat/spacer

Macrophage scavenger receptor

In 3D, the cystine c-c bridge explains why cLS (underlined) is read in reverse sense. Conclusion: Marek's virus 132 bp repeat may be a viral LDLR, which binds to atherogenic cholesterol. This virus must be researched in human atherosclerosis cases and in HIV-1 infected patients with atherosclerosis and/or lymphoma. A vaccine may be designed with this epitope.

Communication CD A006

Anti-tuberculosis vaccine: Molecular homology between Mycobacterium Tuberculosis,HIV-1 Gag and human gamma-interferon (γ-IFN) active site.

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Tuberculosis complicating AIDS is a major health public problem, particularly in poor underdevelopped countries. BCG is only partially active, the discovery of an efficient anti-tuberculosis vaccine remains a difficult challenge, not solved yet. Objectives: We tried to discover a major crucial protective epitope in Mycobacterium Tuberculosis for vaccine design.

Methods: Comparison of amino acid sequences of M. Tuberculosis, M. bovis (Calmette

Guérin Bacillus), human γ-interferon and HIV-1 (BRU, LAV) Gag p17.

Results: We found previously that HIV-1 gag p17 amino acid sequence was homologous to human γ-interferon. *Small characters* means a reverse lecture. The alignment is centered on the γ-IFN active site SDVA; the motif
NGT
binds carbohydrate, GHS binds copper Cu^{++}:

γ-IFN human 12-KKYFN AGHS-DVAD

M. Tuberculosis

HIV-1(BRU,LAV)Gag KKYKLDTGHSSQVSQNY/PIVQNIIKEWRDLE V

Conclusions: To design an anti-tuberculosis vaccine necessitates the deciphering of some major, crucial function of M. Tuberculosis. By basing our research on Casanova's discovery that a mutation in γ-IFN receptor was a susceptibility factor for BCG inducing lethality in infants, we found a crucial "Achilles' heel" in the M. tuberculosis genome, as its protein is a molecular homologue of (precisely) human γ-IFN, a cytokine absolutely necessary for a good macrophage function and HIV-1 Gag. A recombinant M. Tuberculosis "γ-IFN-like" protein or an epitope presented by Heat Shock Protein to dendritic cells (Srivastava P.) could be good candidates for vaccination against tuberculosis.