MHC genes in Invertebrates: The Echinodermata

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Abstract

The MHC is a set of genes that codes for cell surface proteins essential for the acquired immune system to recognize foreign molecules in vertebrates and MHC II gene was described in Echinodermata for the first time. For the present time, MHC Class I gene was not found in a significant manner so for concluding the existence of MHC I gene in Echinodermata, further studies will be necessarily done.

Keywords: *Echinodermata; Invertebrates; MHC Genes*

Introduction

As Janeway CA [1] wrote in 2001, "The function of MHC molecules is to bind peptide fragments derived from pathogens and display them on the cell surface for recognition by the appropriate T cells. The consequences are almost always deleterious to the pathogen-virus-infected cells are killed, macrophages are activated to kill bacteria living in their intracellular vesicles, and B cells are activated to produce antibodies that eliminate or neutralize extracellular pathogens. Thus, there is strong selective pressure in favor of any pathogen that has mutated in such a way that it escapes presentation by an MHC molecule. Two separate properties of the MHC make it difficult for pathogens to evade immune responses in this way. First, the MHC is polygenic: it contains several different MHC class I and MHC class II genes, so that every individual possesses a set of MHC molecules with different ranges of peptide-binding specificities. Second, the MHC is highly polymorphic; that is, there are multiple variants of each gene within the population as a whole. The MHC genes are, in fact, the most polymorphic genes known.

Because of the polygeny of the MHC, every person will express at least three different antigen-presenting MHC class I molecules and three (or sometimes four) MHC class II molecules on his or her cells. In fact, the number of different MHC molecules expressed on the cells of most people is greater because of the extreme polymorphism of the MHC and the codominant expression of MHC gene products.

The term polymorphism comes from the Greek poly, meaning many, and morphe, meaning shape or structure. As used here, it means within-species variation at a gene locus, and thus in its protein product; the variant genes that can occupy the locus are termed alleles. There are more than 200 alleles of some human MHC class I and class II genes, each allele being present at a relatively high frequency in the population. So, there is only a small chance that the corresponding MHC locus on both the homologous chromosomes of an individual will have the same allele; most individuals will be heterozygous at MHC loci. The particular combination of MHC alleles found on a single chromosome is known as an MHC haplotype. Expression of MHC alleles is codominant, with the protein products of both the alleles at a locus being expressed in the cell, and both gene products being able to present antigens to T cells. The extensive polymorphism at each locus thus has the potential to double the number of different MHC molecules expressed in an individual and thereby increases the diversity already available through polygeny.

In addition to the highly polymorphic 'classical' MHC class I and class II genes, there are many genes encoding MHC class I-type molecules that show little polymorphism; most of these have yet to be assigned a function. They are linked to the class I region of the MHC and their exact number varies greatly between species and even between members of the same species. These genes have been termed MHC class IB genes; like MHC class I genes, they encode β2-microglobulin-associated cell-surface molecules. Their expression on cells is variable, both in the amount expressed at the cell surface and in the tissue distribution".

In human, the main function of major histocompatibility complex (MHC) Class II molecules, is to present processed antigens which are derived primarily, from exogeneous sources.

Constitutive expression of MHC Class II molecules, is also confined to professional antigen- presenting cells (APC) of the immune system [2].

Since, we have discovered the IPA (Invertebrate Primitive Antibody) [3-6], to acquire a better understanding of the invertebrate immune system , it seemed useful to look for MHC genes (HLA-DRB1 gene) (HLA-C gene) in invertebrates with *Ophiocomina nigra* (Ophuirids), *Antedon bifida* (Crinoïds) as model of studies. On the other hand we'll have a look on a MHC Class I gene (HLA-C gene) corresponding to a molecule which is a heterodimer consisted of a heavy chain and a light one (beta-2 microglobulin).

Materials and Methods

Animals: *Ophiocomina nigra* (Ophuirid) *Antedon bifida* (Crinoïd) were obtained at the station of Biologie Marine of Roscoff, France. Obtention of ophuirid and crinoïd mRNA: Digestive coeca were excised from their bodies and mRNA was obtained from Uptizol (Interchim) then quality controls were operated [7].

Sequencing: Sequencing was made on Illumina Next Seq 500 with paired-end: 2. 75 bp. Transcriptome was assembled from RNA-Seq fastq files using Trinity v2.1.1 [8] with default parameters. A BLAST database was created with the assembled transcripts using make blast dB application from ncbi-blast+ (v2.2.31+). The sequences of transcripts of interest were then blasted against this database using blastn application from ncbi-blast+ [9] with parameter word_size 7.

Results

MHC gene Class II appears in the genome of *Ophiocomina nigra* and *Antedon bifida* one, in a significant manner. The transcriptomes are given in the following tables, with the sequences just after. First, *Ophiocomina nigra* results show the"HLA-DRB1" transcriptome which possesses a short sequence but a specific one.

Query ID	Quer Name	SubjectID	Identity (%)	Length	Mismatch	Gap open	Query cover (%)	E-value	Bitscore
NM_002124.3	HLA-DRB1	TRINITY_DN4807_c1_g1_i1	90,77	65,00	3	2	5,00	1,00E-15	84,20

>TRINITY_DN4807_c1_g1_i1

5'CATATAGTTTAGGGGGGTTATAAAAAAATGACTCCGGTTACTGACATATTTGGGACCCCAA
CTGTCCAAAGAAAATTATAGCCCCTATAAATTATAATTTATTAATTTTTGTTTTCTCTTG
TATAGGGACCAGAGCCAATCCCACTGGAAGTTAGGGCACGAGCAGTCAAAGACCAATTTT
AAATGTAAAAAAAAAAAAAAAAAAAAATAAAAAATTAAAAAAAAAAAAAAAAAAAATAAAA
AATTAAAAAAAAAAAAAAAAAAAATAAA3'

Secondly with *A bifida*

We find the transcriptome called HLA-DRB1 Antedon bifida with the following e-value, identity, bitscore

QueryID	Query Name	SubjectID	Identity (%)	Length	Mismatch	Gap open	Query cover (%)	E-value	Bitscore
NM_002124.3	HLA-DRB1	TRINITY_DN20232_c5_g3_i1	83,05	59	9	1	5,00	4,00E-06	52,80

The sequence in 5'-3' shows also a short one as for the ophuirid: *Ophiocomina nigra* but remains higly specific as following:

>TRINITY_DN20232_c5_g3_i1

5'GCATGCCTGTAATCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATCACTTGAACCCAGGA
GGCAGAGGTTGTGGTGAGCCGAGATCATGCCATCGCACTCCAGCCTGGGCAATAAGAGCG
AAACTCCGGTCTCAAACAAACAAACAAAAAACAAAACAAAAACAAACAAAAAACAAAACA
AAAACAAACAAAAAACAAAACAAA3'

MHC Class I gene was not found, at least in a significant manner (the e-value was not significative).

Conclusion

It is obvious that MHC class II gene (HLA-DRB1 gene) exist in Echinodermata, at least in Echinodermata which possess a sophisticated immune system as Asterids, Ophuirids, Crinoïds. It would be interesting also to study MHC system in Echinodermata which present only innate immune response as Echinids, Holothurids [10].

The HLA-DRB1 gene is a part of a family of genes called the human leukocyte antigen (HLA) complex.

The protein encoded by this gene belongs to the HLA class II beta chain paralogues. The class II molecule is a heterodimer consisting of an alpha (DRA) and a beta chain (DRB), both anchored in the membrane. It plays a central role in the immune system by presenting peptides derived from extracellular proteins to T helper cells. Class II molecules are constitutively expressed in professional antigen presenting cells (APC: B lymphocytes, dendritic cells, macrophages) and could be induced in non-professional APCs. DRB1 is expressed at a level five times higher than its paralogues DRB3, DRB4 and DRB5. DRB1 is present in all individuals. Allelic variants of DRB1 are linked with either none or one of the genes DRB3, DRB4 and DRB5. There are 4 related pseudogenes: DRB2, DRB6, DRB7, DRB8 and DRB9.

We try now to look for MHC class I genes in Ophuirids and Crinoïds.

The HLA-C gene (we looked for) belongs also to the HLA complex: it helps the immune system to distinguish the body own proteins from proteins made by foreign invaders such as viruses and bacteria [11-13].

Although all efforts to find in Invertebrates a Major Histocompatibility Complex System have been unsuccessful, we find today, for the first time, MHC class II gene (HLA-DRB1 gene) in Echinodermata: It's of great novelty. It is a fundamental discovery in the domain of Comparative Immunology.

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