INFLUENCE OF MAJOR HISTOCOMPATIBILITY COMPLEX (MHC) ON HUMAN MATING PREFERENCES

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ABSTRACT

Several studies related to vertebrates have revealed that highly polymorphic genes within the Major Histocompatibility Complex (MHC) may play a role in mate choice. Females gain direct or indirect fitness benefits by choosing between males with traits that are expressed from good genes, as females can obtain good genes for their offspring by mating with males whose genes are compatible or complementary to their own. There is a tendency for humans to prefer MHC-dissimilar mates, as it would favour the production of heterozygous offspring who would be more resistant to pathogens. This phenomenon has been reviewed on the similar concepts of the influence of MHC genes on human mating preferences, with potential but largely unknown in offspring fitness. The qualitative method can include surveying and interviewing people about their mate choices i.e. females select males with heterozygosity MHC genes over males with homozygous MHC genes. Chi-square test can be performed for statistical analysis. Mating with a MHC dissimilar individual can produce MHC heterozygous offspring that has strong immunocompetence against several parasite types. A heterozygous MHC gene combination has more capability to identify rapidly evolving parasites, which can escape recognition by immune systems containing common alleles.

Plusieurs études reliées aux vertébrés ont révélé que les gènes extrêmement polymorphes au sein du complexe majeur d'histocompatibilité (MHC) peuvent jouer un rôle dans le choix d'un partenaire. Les femmes tirent des avantages directs ou indirects de valeur sélective en choisissant entre les hommes dont les traits sont exprimés avec les bons gènes, comme les femmes peuvent obtenir de bons gènes pour leur progéniture par accouplement avec des mâles dont les gènes sont compatibles ou complémentaires à leurs propres. Il y a une tendance pour les humains de préférer les camarades MHC-dissemblables, car ceci favoriserait la production de descendants hétérozygotes qui seraient plus résistants aux pathogènes. Ce phénomène était étudié sur les concepts similaires de l'influence des gènes du MHC sur les préférences d'accouplement humaines, avec un potentiel largement inconnu dans la valeur sélective de la progéniture. La méthode qualitative peut comprendre une enquête et l'interrogation des gens sur leur choix de partenaire, par ex. les femelles choisissent les mâles avec des gènes du CMH hétérozygote sur les hommes ayant des gènes du CMH homozygotes. Le test du chi carré peut être effectué pour faire l'analyse statistique. L'accouplement avec une personne avec un différent CMH peut produire la progéniture CMH hétérozygote qui a une forte immunocompétence contre plusieurs types de parasites. Une combinaison de gènes CMH hétérozygotes a plus de capacité d'identifier les parasites qui évoluent rapidement, qui peuvent échapper à la reconnaissance par le système immunitaire contenant des allèles communs.

KEY WORDS

Major histocompatibility complex; human leukocyte antigen.

INTRODUCTION

The Major Histocompatibility Complex (MHC) is the most important genetic marker that is used to examine various forms of adaptive genetic variation, pathogen resistance and associated life history decisions about current and future parental effort (Sommer et al, 2013).

The term "Major Histocompatibility Complex" (MHC) consists of a group of closely related genes (MHC genes) that make up the most important genetic component of the mammalian immune system.

The MHCs expressed by Cytotoxic T cells and antigen presenting cells such as macrophages encodes cell surface glycoproteins that bind antigens derived from pathogens or parasites and present them to T-Lymphocytes which trigger appropriate immune responses. MHC variants influence many important biological functions, including immune recognition, susceptibility to infections and autoimmune

diseases, mating preferences, family recognition by recognizing genes or chromosome (homozygous or heterozygous), pregnancy outcome. These diverse roles and characteristics place MHC genes among the best analyte for studies of the mechanisms and significance of molecular adaptations in vertebrates. MHC variability is thought to be maintained by pathogen driven selection. The heterozygotes are expected to have higher fitness than either parental homozygotes (the genotype AB has a higher fitness than AA and BB) particularly if countered with multiple species or strains of pathogens or parasites because heterozygotic alleles are more diversified and express different MHC molecules, which are more suseptible to recognize antigen (also known as heterozygote advantage) or host parasite interaction as a co-evolutionary arm race, in which pathogen in common, infect the common genotype most, leaving rare genotypes least infected. The host individuals carrying new antigens, which have arisen recently by mutation, will be at an advantage because viruses will not yet have had the time to adapt to infecting the cells carrying a new antigen. This will therefore generate a form of frequency-dependent selection (or time-dependent selection), in which a mutant MHC allele initially has a selective advantage compared to an old allele but the advantage gradually declines with time (Takahata and Nei, 2009). The alleles are favoured when they are rare but selected against when they are common, resulting in a balanced polymorphism. (Sommer et al, 2005).

In humans, MHC is also known as Human Leukocyte antigen (HLA) (Havlicek and Roberts, 2009) and MHC locus is located on the short arm of chromosome number 6 at 6p21.3. The MHC genes encode two classes of MHC molecules, Class I and Class II. These genes play a central role in the activation and development of the immune system, including cytotoxic T-lymphocytes, helper T-cells, macrophages, natural killer cells and antibody-secreting B-cells (Penn and Potts, 1999) (Janeway,1993) (Janeway and Travers, 1994).

Several studies have revealed that highly polymorphic genes within the MHC may play a role in mate choice (Chaix et al, 2008). Females prefer to mate with males carrying dissimilar MHC genes (Penn and Potts, 1999), as MHC heterozygotes express more types of functional MHC proteins than homozygotes and therefore are able to encode a large number of peptides (Havlicek and Roberts, 2009). Since MHC molecules (i.e peptides or protein) are present in the urine or sweat, it provides the odour. Even if proteins denature in urine, the epitope recognized by MHC will be preserved. This allows for MHC molecules to bind to allele-specific subset of peptides and their volatile metabolites (such as COO- acid), which may provide the odourants.

Although, the phenomenon to influence MHC genes on odour is still unclear, but there might be possiblities of the presence of either peptide/protein or volatile metabolites (Singer et al, 1997).

Many studies (Yamazaki et al. 1976; Yamaguchi et al. 1981; Potts et al. 1991) have demonstrated preferences for traits which might reveal genetic quality of prospective mates, because they are sensitive to the degree of complementartity between their own genes and those of potential mates. Therefore, it is difficult to predict the potential influence on offspring fitness, since, HLA haplotype can be discriminated solely through odour, and that human females prefer the odours of HLA-dissimilar over those of HLA-similar males. These include studies assessing visual, olfactory and auditory preferences for traits such as dominance or bilateral symmetry (men having greater bilateral symmetry are selected more often by women than men with lesser bilateral symmetry) that indicates good genes (Pillsworth, 2008). Individual differences in these robust preferences mainly arise from individual variation in shape and reproductive condition. Moreover, another set of surveys have revealed preferences for traits that indicates complementary genes, which focus on discrimination of dissimilarity at genes in the MHC (Roberts and Little, 2008).

EVOLUTIONARY ANALYSIS OF MATE CHOICE

Evolutionary analysis of mate choice in human society is a real challenge, because of the diversity of cultural rules and regulations surrounding human sexual behavior. Heterozygosity brings more evolutionary changes in terms of offspring's immunity. In all species, animals choose their partner on the basis of odour and facial preferences (Roberts and Little, 2008).

 DOI: 10.13034/jsst.v10i2.136

ROLE OF BODY ODOUR PREFERENCES ON MATE CHOICE

The body odour preference on the HLA loci (A, B and DR) after MHC's similar/dissimilar experimental procedure between 44 males and 49 females concluded that the women prefer the odour of MHC-dissimilar men. It was shown that the MHC influences both body odours and body odour preferences in humans and that the womens's preferences depend on their hormonal status. Female and male studies were typed for their HLA-A,HLA-B and HLA–DR. Each male student wore a T shirt for two consecutive nights. The next day, each female subject was asked to rate the odours of six T- shirts. They scored male body odours as more pleasant because their MHC genotype were dissimilar with that of the female and vice versa. Further more the odours of MHC-dissimilar men remind the women more often of their own actual or former mates than do the odours of MHC-similar men. This suggests that the MHC or linked genes influence human mate choice (Wedekind and Penn, 2000).

ROLE OF FACIAL PREFERENCES ON MATE CHOICE

Females found the faces of MHC-heterozygous men to be more attractive than faces of homozygotes. This lends further support to the idea that heterozygosity in the MHC may be important in mating decisions. This preference for heterozygosity might not be MHC specific but could rather arise through a general eschewal of relatively inbred males (or those with high average homozygosity at many loci), provided that MHC homozygosity is correlated with inbreeding and any associated deleterious effects (Roberts and Little, 2008).

METHODOLOGICAL APPROACHES

Based on published scientific literature, certain hypotheses and theories can be generated by conducting experiments and stastistical tests.

Hypothesis 1:

Females select males with heterozygous MHC genes over males with homozygous MHC genes for mating. If MHC genes selectively signal for some phenotype (odour and facial preferences) then these phenotypic characters can act as a biomarker for females to select over MHC dissimilar males.

Null hypothesis 1: Females do not show mating preferences for males having heterozygotic MHC genes.

Alternate hypothesis 1: Females show mating preferences for males having heterozygotic MHC genes.

Experimental Plan

A large pool of females and males with known gene sequences at the MHC loci can be taken and the criteria for sexual selection will be defined. This includes phenotypic attributes like facial attractiveness, body odour and healthy skin. The females will be asked to rate males on the basis of these attributes.

This study can be done by selecting large pool of males with different heterozygosities at MHC loci. The males will be allowed to wear a shirt for two consecutive nights. After two days, female volunteers will be asked to score the male odours for their mating preferences. The scores will be given from 1 to 3.

Score - 1: Do not want to mate with or not attractive

Score - 2: Slightly attractive

Score - 3 :Very attractive

Hypothesis 2:

Offspring of heterozygotic males at one of the three loci of MHC (A, B and DR) genes are more viable and immunocompetent as compared to homozygous males.

Null hypothesis 2: Immunocompetence and viability of offsprings are not related to heterozygosity of MHC genes.

Alternate hypothesis 2: Offspring of heterozygotic males at one of the three loci of MHC genes are more viable and immunocompetent as compared to homozygous males.

Experimental Plan

A large pool of females and males (couples) with known gene sequences at the MHC loci (In humans, MHC locus is located on the short arm of chromosome number 6 at 6p21.3) will be chosen. Offspring of heterozygotic males and homozygotic males will be

compared for viability and immunocompetence by sampling. The molecular mechanism of involvement of MHC genes in the proposed outcome will be explored by sampling.

Group 1: Homozygous Males and Heterozygous females at MHC loci are selected and are allowed to mate.

Group 2: Heterozygous Males and Homozygous females at MHC loci are selected and are allowed to mate.

Offsprings belonging to age group, 2-5 years are taken from group 1 and 2 as this age group shall have both innate and acquired immunity and hence is the desirable age group for assessment. 10 ml blood (10 ml of blood contains millions of T cells) is taken out and T cells are sorted. T cells are selected as they are the only cells among the other specialized cells of the immune system (such as B cells, neutrophils, monocytes and macrophages) which contain peptide chain that bind with MHCs. Sorting is done with the help of specific antibody using Fluorescence-Activated Cell Sorting technique (FACS). It is an excellent method of sorting the heterogenous mixture of biological cells and provides fast, objective and quantitative recording of Fluorescent signals from individual cells in addition to physical separation of cells. Whole set of RNA including mRNA from the sorted T cells are extracted and followed by High Througput Sequencing or Next generation Sequencing through Next Generation Sequencing Catalog (NGS Catalog) data base. These sequenced RNAs are then screened for variety of known antigens.

Greater the dissimilarity (heterozygosity), greater is the immunocompetency of the individual. This means AB (heterozygous) will be more immunocompetent than AA or BB (homozygous).

Statistical Analysis plan

Chi-square test will be used to determine whether there is a significant relationship between two independent variables i.e. mating preference and heterozygous MHC genes.

A significance level of 0.05 or 5% will be chosen by Degree of Freedom of Chi-square test.

Chi-Square Distribution Calculator will be used to assess the probability associated with the test statistics.

Predicted Outcomes

MHC dependent sexual selection or mating preferences can be justified as the role of MHC genes can be found in MHC dependant mating preference. Also, gene loci responsible for the phenotype can be estimated.

Faces of men who are heterozygous at all three loci will be judged more attractive and healthy by women than faces of men who are homozygous at one or more of these loci. More symmetrical faces with healthy skin will be perceived as attractive than those with asymmetrical faces.

Offsprings of heterozygotic males will be more viable and immunocompetent in comparison to that of homozygotic males. MHC Protein (Immunoglobulin (Ig) like structure) increases immunity and viability that can be sequenced for further use in future.

DISCUSSION

Role of MHC genes can be found in mating preferences and their product (protein) responsible for the resulting phenotype is already known. The traits, which are selectively chosen by females through sexual selection, can be used to enhance the innate ability of the body to fight against multiple pathogens. At present, mutations among the pathogens may cause the human body to be unable to recognize them as foreign. Hence, if heterozygosity increases, the ability to recognize the pathogens will also be enhanced. Further, the information about heterozygosity (at MHC genes) and increased immunocompetence and viability can be utilized to increase immunity in normal children, as heterozygous MHC genes expresses different MHC proteins for immunoresponse against pathogen. Also, in future, several autoimmune disorders (Grave disease, R. artheritis, Sjögren's syndrome) can be treated with the help of bioengineering by altering these specific gene loci at MHC genes (Roberts and Little, 2008).

 DOI: 10.13034/jsst.v10i2.136

CONCLUSION

The published studies described in this review examine mate preferences over mate choice. Most studies evaluate preferences in a laboratory setting with a sample of participants judging and rating stimulus sets under tightly controlled conditions, often within the context of an imaginary situation. Participants are usually drawn from an age-restricted sample of young adults, commonly university students around 18-22 years old using age-matched stimulus sets. Such studies measure idealized preferences, therefore, they are an estimate of the kind of choices an individual would make, unshackled from the constraints of the real world. However, there is a palpable need for more research in real couples over the mate choice, to demonstrate that sometimes subtle preferences survive in reality, to estimate their magnitude and to explore interactions with other effects.

Therefore, a more sensitive approach is required. In terms of indirect benefits through offspring fitness and correlating with choice of compatible genes, variables that might be illuminating in future work could include difficulties in conception, incidence of miscarriage, infant birth weight and infant health. Infact the degree of HLA-similarity within couples (either at specific loci such as HLA-B and HLA-C or across the HLA region) has been linked to elevated incidence of foetal loss and longer inter-birth intervals.

ABBREVIATIONS

MHC- Major Histocompatibility Complex

HLA- Human Leukocyte antigen

NGS – Next Generation Sequencing

FACS - Fluorescence-Activated Cell Sorting

ACKNOWLEDGEMENTS

I would like to show my gratitude to my instructor, Dr Rachel Walsh for guiding me and enhancing my knowledge during the summer program at Stanford University, USA. I also wish to express my sincere thanks to Mr. Jatin and Mr. Pranjil for their comments on an earlier version of this manuscript.

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