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Some biological features of Mollicutes

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ABSTRACT. *Mycoplasmas* are a bacterial group that is classified in the Mollicute class which includes *Mycoplasmas, Spiroplasmas* and *Acholeplasmas*. One hundred and seventy six species have been described in this group. Mycoplasmas are the smallest self living prokaryotes, they do not have a bacterial wall, their genomic size ranges from 577 to 2220 bpk, they are nutritional exigent so it is hard to culture them, but the development of molecular biology techniques has let us detect more mycoplasmas in different hosts. *Mycoplasmas* have been associated to acute and chronic diseases mainly in animals and humans while spiroplasmas have been found in arthropods, plants and flowers producing or not damage.
Some recent studies have shown the role of some structural components of *Mycoplasmas* in pathogenesis, such as cytoskeleton proteins and adhesins, and the influence of some genetic characteristics on the development of an infectious disease.

Key words: *Mycoplasmas,* chronic diseases, cytoskeleton.

RESUMEN. Los *Micoplasmas* son un grupo de bacterias que pertenecen a la clase Mollicutes, la cual comprende a los *Micoplasmas, Spiroplasmas* y *Acholeplasmas*. Se han descrito 176 especies y se caracterizan por ser los procariontes más pequeños de vida libre que existen, carecen de pared celular, el tamaño de su genoma oscila entre 577 y 2220 kpb, son exigentes desde el punto de vista nutricional y por lo tanto difíciles de cultivar, por lo que el desarrollo de técnicas de biología molecular ha permitido su detección en un mayor número de hospederos. Los *Micoplasmas* se han asociado a enfermedades agudas y crónicas en animales y el hombre principalmente, mientras que los spiroplasmas se han encontrado en los artrópodos, plantas y flores, causando o no daño.
Algunos estudios recientes han mostrado el papel que juegan algunos componentes estructurales de los *Micoplasmas* en la patogenicidad, tales como proteínas relacionadas con el citoesqueleto y las adhesinas, así como la influencia que tienen ciertas características genéticas en el desarrollo de una enfermedad infecciosa.

Palabras clave: *Micoplasmas*, enfermedades crónicas, citoesqueleto.

INTRODUCTION

Mollicutes is a class of microorganisms which includes 176 species. These microorganisms show special features that make them different to bacteria and even between them[36] (Table 1). Mollicutes are the smallest cell free living bacteria that are able to replicate by themselves. Their genome ranges from 577 to 2220 Kbp.[3] They lack of cell wall so they are pleomorphic, their colonies have the typical "fried egg" form, showing a dense central zone. Mollicutes have different habitats including insects, plants, animals and humans.[33]

Mollicutes have been studied in different aspects like their interaction with the immune system,[6] macrophage activation,[25] cytokine induction[23] and the evasion of the immune response by surface components,[37] these studies have lead us to a better understanding of their pathogenicity. Some human *Mycoplasmas* are able to penetrate host cells and are considered as cofactors of AIDS.[5] *Spiroplasmas*, *Acholeplasmas* and *Anaeroplasmas* play important roles as pathogens of different hosts.[11]

The main purpose of this review is to let you know some recent studies of Mollicutes using animals models, their isolation from clinical cases and from their hosts, showing their importance as pathogenic agents.

MORPHOLOGY AND STRUCTURE

Mollicutes are surrounded by a plasmatic membrane, because of the lack of a cell wall they show different forms including pear cell form, a bowl with a terminal-tip or long helicoidal filaments, these forms suggest the presence of a cell skeleton.[31] Some *Mycoplasmas* are able to move on solid surface, that is the case of *Mycoplasma pneumoniae* that posses motility and chemiotactic activity but the genes involved in these activities have not been studied at all.[22]

Spiroplasmas have helicoidal morphology and motility. These functions have relationship with the presence of fibers in their cytoskeleton, these fibers are proteins of 59 Kda, the gene that codifies this protein has been cloned.[38,45]

The genomic analysis of *M. pneumoniae* has let us identify and do the molecular characterization of several proteins that are involved in the architecture of the cytoskeleton. Some of these proteins are adhesins (P1 and P30), others are accessory proteins (HMW1, HMW2 and HMW3), they keep the distribution and position of adhesins in the membrane. P65 and P200 proteins share structural features with HMW1 and HMW3, suggesting that they are part of the cytoskeleton of *M. pneumoniae*.[29,30]

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Cytoskeletal proteins show different migration patterns when electrophoresis is performed, probably because of a proline rich part in the molecular structure.[29]

Mollicutes do not differ from prokaryotes in the way they divide, they do binary fission. In the typical binary fission, the cytoplasm division take place at the same time that the genomic replication, but in *Mycoplasmas*, cytoplasmic division may be delayed once the genomic replication have occurred, including the formation of multinucleus filaments.[31] The mechanisms that rules cellular division in Mollicutes have not been completely studied, but the genomic information that is now available has helped to analyze and evaluate their structure.

One non motile mutant of *Spiroplasma citri* was generated using the transposon Tn 4001, this transposon was inserted in the *Scml* gene, the gene was obtained from a motile wild strain inserted in *Spiroplasma citri*. Transfection of the non motile mutant with the recombinant plasmid restores motility suggesting that the product of gene *smc1* is involved in the motility of *Spiroplasma citri*.[18]

GENOME AND COMPOSITION

Although *Mycoplasmas* posses a small number of genes compared with prokaryotes they are free living microorganisms. It is probably that mycoplasmas evolved from gram positive bacteria and during evolution they lost the ability to synthesize cell wall,[35] but they kept the ability to synthesize other cell structures. When we compare *Haemophilus influenzae*, *M. pneumoniae* and *M. genitalium* we observed that *Mycoplasmas* have a less percentage of genes involved in the synthesis of essential amino acids, they also show deficiency in the genes that codify the energetic metabolism but genes involved in the replication, transcription and translation are in greater percentage than in *H. influenzae* (Table 2). There is intraspecific variation in the genomic size in *Spiroplasma* that is promoted by the insertion of viral sequences that is the case of *Spiroplasma citri* in which the viral sequence is 150 Kb.[2]

Mollicutes have a small and non uniform G + C content. *M. pneumoniae* genes that codify for P1 and OERG adhesins show a great G + C content (56 % mol) while in other replications extremes there is a small G + C content 26 % compared with the average of 40 % of G + C (3, 16). This variation is important from the phylogenetical point of view because it means that genes are conserved for the synthesis of RNAr and RNAt and the possibility of an exogen origin of the genes that codify the synthesis of adhesins.[17]

Spiroplasmas and acholeplasmas are frequently infected by virus (phages) while *Mycoplasmas* are infrequently infected.[48] One of these lisogenic virus that infect mycoplasmas is MAV1, it infect *M. arthritidis* enhancing its ability to induce arthritis.[43] The genome of these viruses ranges from 4 to 40 Kb.[7]

The presence of plasmids has only been reported in *Spiroplasma citri* and *M. mycoides* but the biological role have not been determined.[20,21]

The decrease in the genetic information of *Mycoplasmas* is probably the result of their parasitic way of life, although they have developed special components that attack host cells and let them survive.

ECOLOGY AND HABITATS

There is an increasing list of host for Mollicutes because they are widely distributed in nature, they infect humans, mammals, birds, fishes, insects and plants.

New molecular techniques have led to an easier identification and classification of new species and strains (Table 1).

Table 1. Representative properties of the Mollicutes.

Family (Species number)	Genome size (kpb)	G + C Content (mol %)	Requirement of cholesterol	Host
Mycoplasmataceae (108)	577-1350	23-40	+	Human, animals
Spiroplasmataceae (50)	780-2220	24-31	+	Plants, insects
Acholeplasmataceae (13)	1500-1650	26-36	–	Animals, plants, insects
Anaeroplasmataceae (5)	1500-1600	29-34	+	Ovine and bovine rumen

Data were taken from Weisburg W.G. *et al.*,[44] Bové J.M.[3] and Razin S.[36]

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Table 2. Comparison of the genetic participation in the biological processes in prokaryotes.

Biological function	Identified genes (%) *H. influenzae*	*M. pneumoniae*	*M. genitalium*
Amino acids synthesis	68 (4.0)	0 0	
Cofactors synthesis	69 (4.0)	8 (1.2)	8 (1.7)
Cellular membrane synthesis	105 (6.2)	54 (8.0)	30 (6.3)
Fatty acids and phospholipids	40 (2.3)	9 (1.3)	8 (1.7)
Energy metabolism	142 (8.3)	45 (6.6)	37 (7.7)
Transport	123 (7.2)	44 (6.5)	34 (7.1)
Replication	87 (5.1)	46 (6.8)	32 (6.7)
Transcription	27 (1.6)	13 (1.9)	13 (2.7)
Translation	25 (7.3)	99 (14.6)	99 (20.6)

The number in parenthesis indicates the total percentage of identified genes. Based on the data from Fleischmann *et al*.,[8] Fraser *et al*.[10] and Himmelreich *et al*.[17]

Some studies support the presence of structures similar to *Mycoplasmas* in animal tissues including humans. Wirostko´s describe the presence of fastidious microorganisms that produce uveitis and probably other human diseases, they have been identified so Mollicutes.[19]

The first *Mycoplasmas* isolated from Bartholin glands of humans was *Mycoplasma hominis*, other species have been isolated from humans being *Mycoplasma penetrans* the latest to be described[26], encouraging microbiologist to search.

Mycoplasmas show tissue and host specificity as a result of their nutritional needs and parasitic way of live. Although this host specificity some human *Mycoplasmas* may induce experimental infections in animals, that is the case of *M. pneumoniae* that is able to induce experimental tract infections in hamsters and a natural pneumonia in humans.[9]

The natural habitats of *Mycoplasmas* are the respiratory and urogenital tracts, eyes, mammary glands and joints. Some *Mycoplasmas* enter the body using the respiratory or urogenital tract and then they reach other tissues that is the case of *M. pneumoniae* and *M. genitalium* that have been isolated from urogenital and respiratory tract.[10,16]

The increasing number of patients with immunodeficiencies associated with hipogammaglobulinemia like AIDS and the treatment of patients with immunosuppressive drugs have favored the isolation of *Mycoplasmas*.

Some *Mycoplasmas* and *Ureaplasmas* are considered normal flora of the urogenital tract but recently they have been isolated from blood of patients with AIDS or immunosupressed patients who are more susceptible to suffer urogenital infections by *Mycoplasma hominis* and *Ureaplasma urealyticum*. The bacteria may invade the respiratory tract and joints producing damage.[12,28]

The development of new techniques of molecular biology have improved the diagnostic of *Mycoplasma* infections because these microorganisms are fastidious and their identification can only be performed by PCR amplifying genes of the 16S subunit of RNAr.[24,36]

Spiroplasmas are motile and show helicoidal morphology, they are frequently isolated from intestine, salivary glands, homocele of insects and the surface of plants and flowers.[46,13] *Spiroplasma melliferum* and *Spiroplasma apis* are pathogenic for bees, they cross the intestine barrier reaching hemolinfa where they reproduce and induce death of their host.[4] Spiroplasma have also been reported in *Aedes aegypti* mosquito reducing the fertility of the insects, opening the possibility of their use as biological control of mosquito.

Several neotropical species of fruit flies (Drosophila) and cockroaches are susceptible to the infection by *Spiropalsma poulsonii* and *Spiroplasma floricola* respectively. *Spiroplasma* may establish a mutualism relationships.[27,47]

Spiroplasma mirum was isolated from rabbit ticks and is considered pathogenic to chicken embryos, new born rodents and adult rabbits. SMCA strain induces a high incidence of cataracts in new born rodents, while GT-48 strain induces fatal encephalitis.[39,40]

Acholeplasmas have been isolated from feces of healthy horses and feces of pathogen free rabbits.[1, 15] Acholeplasmas have also been reported in hemolinfa of fire flies, being the first report of a *Spiroplasma* in the homocele of insect.[41] *Anaeroplasmas* have only been isolated from bovine and ovine rumen.[32]

CONCLUSSION

Mycoplasmas are bacteria with special genetic features that make them different of other prokaryotes, these characteristics let them interact closely with their host producing plant, insect, animal and human infections.

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