

## Cells without an External Plasma Membrane

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### ABSTRACT

Nearly all eukaryotes have an exterior plasma membrane with glycoproteins on the outer leaflet however. The exception may be the intracellular microsporidian parasites which have an outer membrane with an exterior leaflet bearing only cytoplasmic proteins. How can this be? The initial stage, the sporoplasm, is injected into a host cell and its outer membrane appears to be derived from a cytoplasmic organelle referred to as the extrusion apparatus. The introduced microsporidian cell retains this organelle membrane with its outer leaflet of cytoplasmic proteins throughout the remainder of its life cycle. A conventional plasma membrane does appear but only during spore wall formation and this membrane remains interior to the microsporidian while it is engaged with the development of the external wall whereas, the outside cytoplasmic membrane remains exterior to the developing spore wall. The intracellular microsporidia, which locate within the host cytoplasm, has its external membrane leaflet in direct contact with the host cytoplasm. All the cytoplasmic proteins on this exterior membrane of the microsporidian are believed to be of host origin and, therefore it is not surprising that the parasitic cell does not yield a detectable reaction either by the host cell or the host organism. This study is based on observations on the microsporidians *Spraguea amricanus*, *Anncaliia algerae*, *Ameson Michaelis*, and *Thelohania sp.*

**Keywords:** Exterior cytoplasmic membrane; Plasma membrane; Glycoproteins

### INTRODUCTION

While eukaryote cells are always thought to have an outer plasma membrane bearing an external surface coat produced by Golgi, here is an exception the microsporidia. These intracellular parasites have an outer membrane which is cytoplasmic and not a plasma membrane the microsporidian cell outer membrane has an external leaflet bearing only cytoplasmic proteins.

### LITERATURE REVIEW

#### How can the microsporidian cell have an external membrane with an outer leaflet of cytoplasmic proteins?

It begins with the infective spore stage which functions as a missile for when the spore is activated. It launches a long, fine tube through which the spore contents (sporoplasm) transfer into a host target cell. The spore has within it an extrusion

apparatus organelle with a membrane rich polaroplast. When the protein tube is formed, the membrane from the polaroplast passes out of the tube and forms at the end of the tube a membrane sac into which the sporoplasm of the spore enters [1]. Earlier studies have shown this membrane sac is derived from the polaroplast organelle and it becomes the outer membrane of the sporoplasm. The microsporidian does develop an internal plasma membrane during spore wall development however, when the spore discharges, it leaves the old plasma membrane behind and the sporoplasm cell acquires its outside membrane from the polaroplast organelle.

#### Are the proteins on the outer membrane all cytoplasmic?

Yes, cytoplasmic proteins are always confined to the cytoplasmic domain. Hence the following cytoplasmic proteins have been identified from the outer membrane on the sporoplasm stage or the exospore wall of the spore stage intermediate filaments,

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dynactin components, dynein, tubulin, clathrin, calmodulin, some kinases, channel proteins, and the cell adhesion molecule cadherin and its associated molecules, the catenins.

### **Are the cytoplasmic proteins really on the outer leaflet of the exterior membrane on the microsporidian cell?**

The answer is yes with reference to the proteins listed above. It is well known that intermediate filaments (IFs) are cytoplasmic proteins and these were on the cytoplasmic leaflet of the microsporidian membrane along with their associated cadherin and catenins [2]. These proteins were identified on the outer membrane of spore forming stages of a number of different species of microsporidians, particularly those that parasitized muscle cells. Microtubules have also been reported to attach to the outside of the sporoplasm cell, the later trophozoite stages, and the spore forming stages [3]. In order to bind onto membrane, tubulin requires a connection with adhesion proteins coupled to dynein and a dynactin component [4]. Recent studies have reported the binding of labeled tubulin onto the surface of newly discharged sporoplasms. This indicates attachment proteins are also present [5]. In summary, this whole surface is oriented so only cytoplasmic proteins attach and since this surface of the parasite is facing the host cell cytoplasm, it is a rather peculiar situation for both the host cell and parasite.

### **Where do the cytoplasmic proteins come from that are found on the outer membrane on the microsporidian cell?**

They likely all come from the host cell. It has been confirmed that the microsporidian genome does not have the genes for animal cell adhesion proteins such as cadherin and its associated proteins the catenins nor does it have the genes for intermediate filaments. In a recent study, the source of the microsporidian cadherin was looked at by initiating *A. algerae* infections in *Drosophila* stocks which had their cadherin genes labeled with GFP. The study revealed the hosts' labeled cadherin ended up on the outer membrane on the microsporidians in both the sporoplasm and the spore stage [5]. Since even the conserved cytoplasmic proteins across taxonomic groups are slightly different, they should generate a host reaction yet, the cytoplasmic proteins on the surface of microsporidian stages do not trigger any observable response. To test this, the surface and proteins from the outer membrane of the exospores of *S. americanus* were recovered and Western blots were prepared using the immunoglobins of the host animal which had been parasitized for many months. The results showed no detectable response by the host against any of the cytoplasmic proteins from the exospore membrane outer surface. This would indicate all these proteins were likely of host origin [5].

### **Having an external cytoplasmic membrane and an internal plasma membrane?**

From the microsporidian sporoplasm stage until the end of the trophozoite stage, the microsporidian cell has but a single outer membrane bearing surface cytoplasmic proteins. However, at the

onset of sporogenesis, the outer membrane doubles with the inner membrane extends its separation during spore wall synthesis. Chitin, a major component of the spore wall, is assembled by means of chitin synthase, a glycosyltransferase. Since all glycosyltransferases have a Golgi association [6], the inner membrane because of its Golgi affiliation, is by definition a plasma membrane. After the completion of the spore wall, the outside membrane continues to remain attached to the exospore wall while the inner plasma membrane remains attached on the inside of the endospore wall. When the spore discharges at the time of spore activation, the sporoplasm exits the spore and enters into a membrane compartment that comes from the polaroplast component of the extrusion apparatus. The original cytoplasmic membrane remains on the outside of the exospore wall, and the old plasma membrane remains on the inside of the wall of the empty spore [5].

### **Some consequences of having an external cytoplasmic membrane in association with host cells by microsporidians**

For an intracellular parasite confined directly within the cytoplasm of a host cell, the results are apparent on how the microsporidians fare in the host cells. In the lophius host, the target is always a neuron in which the microsporidian can develop into a large colony of spores [7]. But once the parasites reach the spore stage, they remain that way for the life of the animal which can be around twenty years. If microsporidians are so good at remaining undetected by the host animal, how come they don't simply over run the host animal in numbers of parasites? It has something to do with the parasite's cycle. Once the source of energy runs low in the host cell, the parasites convert to spores and tend to remain that way for the life of the host animal. Thus, while nearly all of anglerfish of the genus *lophius americanus* are parasitized by microsporidians, most of the fish carry on and live long normal lives because once the microsporidians are in the spore stage, they remain that way until the end of the host animal. So this may be a good survival adaptation for both the host and the parasites. However, sometimes the host energy reserve is not limited for example, when the host tissue is syncytial muscle, the microsporidians in this tissue sometimes continue to propagate until most of that muscle is converted into microsporidians. That can be pretty tough on the host animal and it has been observed in both mice and men.

And more questions. Sometimes, an intracellular microsporidian colony can grow to large numbers in a domain of the host cytoplasm where there is not a lot of synthetic capability for example, the *S. americanus* parasitism frequently develops in axons of nerve fibers yet, each microsporidian cell within the large colony acquires a rich canopy of host proteins such as cadherins, catenins and the associated intermediate filaments. It would seem the host cell has to be signaled for it to undergo any elevated protein synthesis. How can an intracellular parasite signal a host cell when it is surrounded by only host proteins on its outer membrane? One possibility is the parasites may send molecular activators into the host cytoplasm/nucleus when the initial sporoplasm is transferred into the host

cytoplasm in the first place. The assumption has been that everything is transferred from the spore stage through a tube and into the membrane sac that surrounds the entering sporoplasm. Perhaps that is not the case. There may be signal molecules that do not go into the sac but go directly into the host cell cytoplasm/nucleus and subsequently the host cell's synthesis controls might be altered.

## CONCLUSION

All stages of microsporidians appear to display an outer cytoplasmic membrane which was originally derived from the polaroplast organelle during sporoplasm introduction into the host cell. All the proteins on the exterior surface of this outer cytoplasmic membrane appear to be of host origin and these host cytoplasmic proteins seem to remain in this position with their orientation always towards the host cell cytoplasm. The parasitic cell's exterior cytoplasmic membrane with its outer canopy of host cytoplasmic proteins may provide the ultimate escape mechanism. If this canopy of host cytoplasmic proteins holds up throughout the life cycle for the parasite, the host finds it difficult to respond. It is clearly the way to avoid detection for an intracellular parasite.

## CONFLICT OF INTEREST

None

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