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# Some Infections May Be Endogenous

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**Abstract**

This paper advances a previous hypothesis "Human body may produces bacteria", and proposes that some infections may be endogenous.

It has been demonstrated that the Christensenellaceae, a family in the phylum Firmicutes, is heritable suggesting that human genetic material and gut bacterial material are related and human cells may generate some gut microbes It has also been shown that the fetus is exposed to bacteria prior to birth -without any evidence that they are contaminants or acquired from the environment -suggesting a possible endogenous origin of bacteria in breast milk, meconium, placenta , umbilical cord blood and amniotic fluid.

Malassezia yeasts are not contagious, not culturable from the environment, cannot colonize human skin by inoculation without occlusion and neonate skin is free of Malassezia but is colonized in the first month of life suggesting that they may be endogenous.

Human stem cells seem to be the most likely candidates to produce microbes: This is because they differentiate to epithelial cells and cancer cells and contain the essentials to transform to microorganisms.

Future experimental studies are necessary to validate this hypothesis which may offer a new paradigm to combat opportunistic infections of possible endogenous origin.

## Introduction

Since the introduction of the germ theory, it has been accepted that all infections result from foreign invading microbes [1]. However, a recent hypothesis proposed that human body may produce bacteria [2].

This paper hypothesizes that human stem cells may produce microbes and proposes that some infections are endogenous.

The evidence in support of this hypothesis," Some infections may be endogenous" is based upon diverse observations that will be discussed under four headings:

A. Multi potency of stem cells.
B. The origin of gut bacteria.
C. The origin of bacteria in breast tissue and milk.
D. The origin of Malassezia yeasts.

### Multi Potency of Stem Cells

In multicellular organisms, stem cells are the earliest type of cell in a cell lineage and can differentiate into various types of cells and proliferate indefinitely to produce more of the same stem cell [3]. Epithelial tissues line the outer and inner surfaces of organs throughout the body and harbor stem cells that differentiate to epithelial cells [3].

It has been observed that, perhaps the most important and useful property of stem cells is that of self-renewal (4). Cancer cells may often originate from the transformation of normal stem cells and cancer cells may include 'cancer stem cells' — rare cells with indefinite potential for self-renewal that drive tumori-genesis (4). Stem cells contain a nucleus whereas bacteria have a nucleoid [5]. Using long-term lineage tracing, Lopez-Garcia et al., showed that the loss of a stem cell was compensated by the multiplication of a neighbor cell (5). The rate of stem-cell loss was equivalent to the rate of cell division, indicating that symmetric cell division was the rule for gut stem cells [6].

### The Origin of Gut Bacteria

It has been shown that some gut bacteria (The Christensenellaceae, a family in the phylum Firmicutes) are heritable [7]. The Christensenellaceae's, relative abundance in the human gut is inversely related to host body mass index (BMI) in different populations making its relationship with BMI the most robust and reproducible link between the microbial ecology of the human gut and metabolic disease reported to date [7].

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Heritable means genetic material is transmitted from a person to his or her offspring. In essence a human- a complex multicellular organism - passes on the genetic material of gut bacteria to his or her offspring. This also means the bacteria are not only part of the human but also produced by human cells and gut stem cells and gut microbes are genetically related. In addition, It has also been demonstrated that human genetics shape the composition of the gut microbiome in concert with environmental factors such as diet and lifestyle [7-14] . Furthermore, it has been demonstrated that variants in single genes (for example, LCT, NOD2 and FUT2) affect the composition of the gut microbiome [14].

It has also been demonstrated that host genetics dictate the composition of gut bacteria and 8 bacterial taxa were identified whose abundances were associated with single nucleotide polymorphisms in the host genome [14].

Nucleoid of bacteria forms a pseudo-compartment that frequently occupies a distinct region within the cell- characterized by the absence of ribosomes - is functionally equivalent to the eukaryotic nucleus [5].

Taken together, the above findings suggest genetic information may be passed on from the nucleus of human cells to the nucleotide of bacteria.

### The Origin of Bacteria in the Fetus

Until recently a medical dogma had prevailed that the fetus was sterile although today we know that the fetus is not sterile [15], amniotic fluid [16,17], meconium [18,19], breast milk [20,21] breast tissue [22] umbilical cord blood [23], contain bacteria. Of importance the unique composition of bacteria of each subgroup is different [24] suggesting that they don't share a common origin. This observation contradicts the entero-mammary translocation hypothesis [25] which proposes that bacteria from maternal gut may represent the common origin of bacteria in breast milk and tissue. In other words bacterial production is local.

### The Origin of Malassezia Yeasts

Malassezia furfur was the first species described within the cosmopolitan yeast genus Malassezia, which now comprises 13 species [26]. Reported isolation rates of these species from healthy and diseased human skin show geographic variations [26]. There is evidence for an association with the host's genetics and with the M. Furfur strains similar to the genetic influences that shape gut microbes [26,27].

Tinea versicolor a Malassezia yeast induced skin disorder is heritable [28-30], not contagious [28,29] and they have not been cultured from the environment [27] suggesting that they may also be endogenous. At birth neonate skin is Malassezia free [31] yet by the end of the first month is colonized by Malassezia [32]. It is very hard to explain this observation without considering the possibility of an endogenous origin partly because Malassezia infections are not contagious; it is difficult or impossible to colonize human skin by inoculation without occlusion [33] and finally Malassezia has not been cultured from the environment [27].

## Discussion

Diverse and multiple observations support the hypothesis that some infections are endogenous however to date there has not been any experimental study to validate this novel hypothesis. The strongest evidence to suggest a possible endogenous origin of microorganisms is the genetic link between humans and some human bacterial and fungal flora such as M. Furfur and The Christensenellaceae.

**Genetic Link Between Humans and Unicellular Organisms**

- Some gut microbes (the Christensenellaceae )are heritable and they are passed on from one generation to younger generations.
- Malassezia furfur yeasts are heritable and they are passed on from one generation to younger generations.
- Both gut microbes and Malassezia furfur yeasts are a part of normal human flora.

It can be argued that the human genetic influences- the heritability of some gut microbes and the observation that human genetics shape gut bacteria -are consistent with the endogenous origin of microbes yet, they may possibly represent influences associated with the host vulnerability to disease, infection or colonization.

It is also possible that the bacteria in breast milk and tissue are not contaminants but, they may originate from the mother. However, this possibility does not seem to be likely because the composition of bacteria in breast tissue and milk, Is different than the composition of bacteria from maternal gut, their proposed origin.

At birth neonate skin is Malassezia free yet by the end of the first month is colonized by Malassezia. It is very hard to explain this observation without considering the possibility of an endogenous origin partly because Malassezia infections are not contagious, it is difficult or impossible to colonize human skin by inoculation without occlusion and finally Malassezia has not been cultured from the environment.

It seems that stem cells differentiate to epithelial cells and cancer cells and are the most likely candidates to produce microorganisms. I t is necessary to experimentally demonstrate that human stem cells may produce microbes.

In summary "human stem cells may produce microbes" is a biologically sound hypothesis that is most likely accurate yet requires further experimental validation. Seems that this hypotheses may pave yet unexplored avenues to treat some opportunistic and burn wound infections.

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### Conflict of interest

Alen J Salerian MD has no conflict of interest.

### Ethics approval

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