The ethical aspects of using synthetic biology to screen for endometriosis

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The realm of medical ethics is highly important when delving into novel means of diagnosing and treating maladies using synthetic biology. Not only should we consider the risks involved with using synthetic biology for medical appliances or treatments, but we should also put the appliance itself under ethical scrutiny. This year, the members of the iGEM Team from Paris-Saclay University in France chose to work on Endometriosis, with their project EndoSeek, by developing a new way of detection for the disease. They worked in a partnership with iGEM Lund (Sweden) to study the Ethics related to their projects: iGETHICS. Both our Universities are members of the EUGLOH (European University Alliance for Global Health).

Endometriosis is a common gynecological disease where cells similar to the endometrium grow outside of the uterus, causing a big amount of pain or infertility in everyday life. 1 in 10 women is affected by the illness but the statistics are underestimated. In fact, the time between the first symptoms and the diagnosis is around 6 to 7 years which is considerable, meaning that today, there are many women who do not know about their endometriosis yet [1].

A woman living her daily life is in her menstruation period.She bleeding and working. Her ovaries hurt, she is bloating, and she is trying to diminish her symptoms with a hot water bottle, heat pads and medication. Unfortunately, the pain experienced by women with endometriosis is often too excruciating for medication to be sufficient. Endometriosis may be very difficult to diagnose by yourself, and even by medical professionals and may have to be invasive, requiring surgery or expensive means of medical imagery. This is why we developed EndoSeek.

When a woman has her period, the endometer that was in the uterus is eliminated through the vagina. When a woman has endometriosis, cells from the endometrium migrate from the uterus to other organs like ovaries, or intestine for instance. These cells are already submitted to the hormonal cycle, and this is one of the causes of the symptoms. In many cultures the illness is associated with fear and taboo. But above all, this illness is very hard to deal with for the patient. The true scope of symptoms include chronic pains, painful menstruation, and infertility among others depending on the woman and the stage of the disease [1] [2].

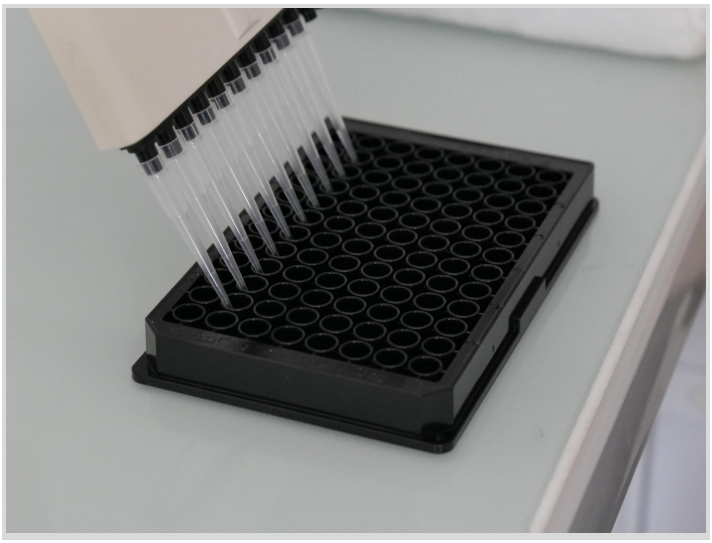
Photo by Sora Shimazaki from Pexels

Needless to say, endometriosis is a tricky disease in need of new effective solutions.

The EndoSeek Team exchanged with gynecologists. Doing so, they recognized that they had to be careful regarding the design of their diagnostic tool, delving into questions about ethical application and use. Screening for diseases allows the patient to detect the disease before any symptoms are apparent.

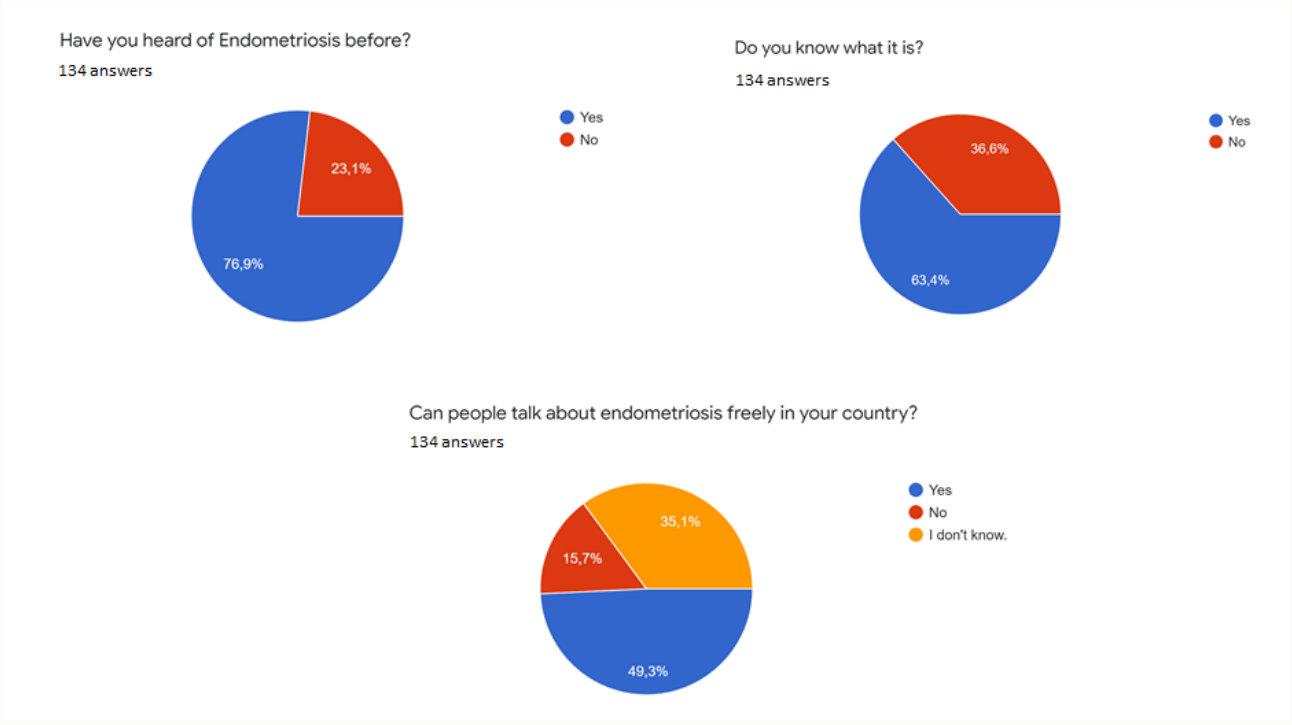
The project involves the detection of miRNA (microRNA), which are non coding small RNAs which allow the regulation of gene expression [5][6]. In cases of endometriosis, certain miRNA molecules are dysregulated, allowing EndoSeek to utilize them in order to diagnose the disease. miRNA constrive a family of biomarkers which allows for an interesting approach of diagnosing. However, the method raises some ethical concern since the tools used to detect miRNA are associated with genetically modified organisms (GMOs)
The use of GMOs in medical solutions is ubiquitous in synthetic biology. Although there are many advantages to solutions using GMOs, there are some concerns regarding the fact that it can be dangerous for instance with all the laboratory biosafety issues. There is

even some debate regarding ethics of the mechanical and instrumental use of biological organisms. The topic of GMOs is explored further in an article written by iGEM Lunds: *The Future of Alzheimer's Prevention: Shedding Light on Probiotics and GMO*, which we invite you to read. [7]



EndoSeek has two main ethical and cultural challenges: dealing with a disease which is laid with taboos and cultural stigma, and using non-conventional means of diagnosing that disease. It therefore seems paramount to investigate the cultural aspects of our project, by getting the public's opinion on the project and topic. For this, we made a survey we spread in the international iGEM community. The results were interesting as a quarter of the respondents had never heard of endometriosis before. Moreover, about one third of the iGEMers do not know what endometriosis is. It is clear that the lack of communication regarding endometriosis is not just about the general population but also about the medical profession. A sizable and significant part of doctors and gynaecologists are not sufficiently aware that much about endometriosis whether it is because they are not trained enough or do not think about it.

It seems paramount to our project to communicate and spread awareness of the disease, especially since the screening tool we're creating may result in the discovery that asymptomatic patients in fact have the disease. Therefore we need to ask ourselves, is it ethical to screen for asymptomatic diseases, or does it simply result in panic and worrying which in itself may be unhealthy?



On the other hand, added grounds are a kind of trivialization and minimization of the pain induced by endometriosis. Pain and especially constant and chronic pain indeed are not self-evident for someone who never experienced it. Moreover, pain is different depending on the person. In 2020, an Australian artist, Eugenie Lee has developed a VR installation artwork dealing with endometriosis pain. The dispositive is a belt giving to the wearer pelvic pain-like sensation. It was tested notably by a gynaecologist and endocrinologist, doctor Andreadis. While trying it, her words were "I didn't realise [how hard it was], now I know. [...] Take this to med schools, strap every doctor and nurse [to it because] it'll make us more empathetic in terms of managing our patients." The point here is not that much about being empathic but about not disparaging pain [8].

Through further conversations with gynecologists specialized in the case of endometriosis, the goal of EndoSeek was settled, and the moral status of the project was decided to be positive. Firstly, early diagnosis is often beneficial when it comes to treating the disease, and even though asymptomatic patients aren't aware of their illness in the current state, they most likely will be in the future. Women with severe endometriosis could benefit even more from early diagnosis as their endometriosis engenders may result in infertility and they might want to freeze their ovocytes.

This added a second layer of ethics onto the project, as the issue of freezing ovocytes and ovarian tissue is controversial. In France, the bioethic laws L.2141-11 states that every person with medical care susceptible to alter the fertility, or for whom the fertility can be prematurely altered, can benefit from collection and conservation of gametes or germinal tissues, to preserve or restore fertility [9]. This law has equivalents in many progressive countries, and the issue with fertility preservation may therefore decided to be settled.

However, the cultural stigma around endometriosis and fertility preservation is still present in many countries. The situation in rural areas in India for example is quite complicated as menstruation is a real taboo issue. So how can women know about endometriosis if they can't even talk about menstruations? [10]

As can be deducted, endometriosis isn't only a disease - it's a societal issue. Developing screening tests for such an issue is controversial, and even more so when the screening tool itself is created using synthetic biology. Our interviews highlighted that EndoSeek requires ethical consideration in the field of medical ethics, cultural adaptation and widespread use of genetically modified organisms. We at iGEM Paris-Saclay are determined to educate and discuss these issues in order to provide a better future for women's health and for biotech innovations.

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About the authors :

Stelina LOIODICE is in her 3rd year of Bachelor's degree in Biology and Health at Paris-Saclay University in parallel with a Magistère of Biology. She is really interested in the field of health and food industry, and she likes microbiology. Stelina wanted to learn more about synthetic biology and this is why she joined the iGEM competition. It was a really great experience !

Eve DO ESPIRITO SANTO is in her 3rd year of Bachelor's degree in History of Arts and Archaeology at the Ecole du Louvre. She joined the competition later. Her interest in the project was mainly about the social impact of our project, the ethics, and obviously the Art related to Endometriosis.

Amiel ABETTAN just finished his Master's degree in engineering and chemistry of biomolecules at Paris-Saclay University. He was mainly working at the lab for our project but he also was invested in our partnership with iGEM Lund.

Mathieu NAIRABEZE just finished his second year of Master's degree in Biology with a speciality in Microbiology and Biological engineering at Paris-Saclay University. He is quite versatile in the team and decided to work on our partnership with iGEM Lund.