Good morning/afternoon/evening, We are representatives of the CityU iGem Team. Thank you for taking the time to do this interview with us.

Our team is working on a synthetic biology project related to the production of variecolin analogues which are compounds with potential therapeutic and antimicrobial properties. We aim to create a series of variecolin derivatives using an Aspergillus fungal host transformed with various P450 genes derived from several different fungi.

Questions:

- Sickness is always the biggest challenge for human beings. Do you think the current drugs/medicines are sufficient to deal with existing illnesses ? (Drug discovery recent situation)

Ans: Drug discovery needs a better platform for drug screening in vitro and in vivo. Current drugs are not sufficient as there may be side-effects. Different individuals may have different response rates. Therefore, patient stratification with personalized medicine will be the future trend.

- Natural products (from plants) are commonly used in drug discovery and development. Do you think it's a good strategy to use natural products in the development of novel drugs?

Ans: Natural drugs will be a fast way to identify drug targets with potential therapeutic effects. More importantly, we need to delineate the underlying mechanisms about how the drugs bring out the effects. After knowing that, more analogs with similar but modified chemical structures can be created and further studied. E.g. the improvement of the drugs' pharmocokinetics, bioavailability and biostability, etc.

- We are aiming to produce novel forms of variecolin analogues using a synthetic biology approach, which are natural products with potential anti-cancer and antimicrobial properties. Do you think this approach could have a positive impact on the drug discovery process and industry?

Ans: I think it has a positive impact on drug discovery. The host can provide the enzymatic machinery to create various analogs of the drugs by modifying the chemical groups. This may help to generate a library of chemical analog drugs with different

modifications for subsequent drug screening process, provided that if all the drug analogs created by the host can be identified one by one.

- If new forms of variecolin analogues are successfully created, do you know of any relevant and reliable tests that could be used to screen for anti-cancer and anti bacterial properties ?

Ans: For anticancer properties, you can add the drugs to cancer cell lines and assess the effects on proliferation of the cancer cells by proliferation assays, MTT assays, etc. Also, caspase cleavage (by Western blots), annexin V assays or trypan blue counting can be used to judge the effects on apoptosis. To validate further in vivo, you can administer the drugs to subcutaneous xenograft models in which the cancer cell lines were subcutaneously injected to immunodeficient mice and the tumor sizes were measured and monitored between the untreated control group and the treatment group.

For antibacterial properties, you can add the drugs to the bacterial culture and monitor the bacterial growth by the optical density measured by spectrophotometry to compare between the treatment and the untreated control groups.

- Do you have any comments or suggestions on our proposed project strategy and project aims?

Ans: This is a good way to develop a biological platform for creating drug analogs by synthetic biology. It is important to identify the drug analogs created and assess their effects on cancer cell proliferation. Pharmacokinetics profiling may be needed. E.g. Toxicity issues of the drug analogs on human cells need to be concerned.

This is the end of our interview. Once again, thank you for your precious time.