[Vincent]

Good afternoon, everyone, today we are going to talk about Lab-on-a-chip.

My name is Vincent, and they are my groupmates Helen and Ka.

Today's presentation consists of four parts.

For the first part, I will introduce what lab-on-a-chip is. For example, its components and advantages.

For the second and third part, we will introduce diagnostic and research applications with different examples.

Finally, we will have a future prospect of this technology.

Now let's start our presentation with the introduction.

So, what is Lab-on-a-chip? By definition, it is a device that integrates micro electromechanical systems that can carry out all stages of biological and chemical processes.

These unique properties enable Lab-on-a-chip in some key features.

For example, Point-of-Care Diagnostics, Biochemical Analysis, Drug discovery and regenerative medicine. Those are the most common features of Lab-on-a-chip.

After introducing the feature of Lab-on-a-chip, now let's talk about what's inside a Lab-on-a-chip device.

As you can see on the screen, there are nine major components of Lab-on-a-chip. Because of time limitations, I will introduce the two most important components of Lab-on-a-chip.

One of them is detector, detectors consist of transducers that acquire physical signals from analyte and transform them into electrical signals for analysis.

Another one is reactor, it maintains and controls a chemical or biological reaction in a controlled environment.

Together with those components, enable Lab-on-a-chip sample handling, mixing and reacting with reagent, as well as separation or detecting analyte.

Why is lab-on-a-chip so important? There are so many advantages of using lab-on-a-chip. It enables miniaturization and integration of complex functions that can automate repetitive laboratory tasks.

Therefore, it reduces reagent consumption and waste generation. Also, it can be more time and cost-effective.

[Helen]

Let me first introduce diagnostic application of LoC. Different diseases can be diagnosed by loc devices. I will focus on one research regarding the diagnosis of chronic kidney diseases.

CKD affects approximately one in ten people globally, which is associated with irreversible kidney function loss. Since this disease progress rapidly, we need renal function assessment and monitoring. Current clinical diagnosis involves chemical analysis using estimated glomerular filtration rate (eGFR) and urine albumin to creatinine ratio (UACR). However, the equipment required are expensive and only available in centralized labs. Different LOC devices are developed to directly measure the level of creatinine and cystatin C in blood and urine.

For example, one LoC device is developed to measure the elevated creatinine level in blood, which is based on electrophoretic separation and conductivity detection. It can be done in an automated manner using a single disposable microfluidic chip and a handheld analyzer. The LOD is ~100 μM, which is sufficient to be used as a screening tool for distinguishing renal insufficiency patient (>100 μM in serum) and healthy subject (60–100 μM in serum). While another one is a LOC device which integrate microfluidic chip with the capillary–gravitational valves to measure creatinine in urine. This chip used the balance between capillary and gravitation forces for sequential fluid delivery, metering and mixing, which can be controlled by battery powered motor or simply operated by hand. The burst pressure of the capillary values could be broken by the gravitational force while the chip was rotated from horizontal to vertical. Other than these two examples, there are still different LOC devices designed for CKD diagnosis.

Why we need LOC technology to perform diagnosis of different diseases? First, compare to conventional method, it has high accessibility. With this small chip, we don't have to send samples to centralized laboratory for analysis. All end users can use this chip manually by themselves which allow regular monitoring at home. Second, by taking advantage of microfluidics, the sample volume required can be reduced to microliter or even nanolitre, which reduce the reagent costs. Moreover, the use of LOC enables higher accuracy in detection like preventing interference by other analyte in the sample since it has better sample processing.

[KA]

Next, I'll talk about the research applications for LoC.

Allow me to introduce what organ-on-a-chip is.

Broadly speaking, OoC is an *in vitro* technique that incorporates live cells onto a chip to simulate certain *in vivo* environments and even entire organs.

For example, the figure on the right here is a capillary network-on-a-chip with a co-culture of endothelium cells and cancer cells. This is to simulate a cancer invasion scenario.

But obviously, culturing human cells is nothing new.

However, conventional 2D *in vitro* approaches do not allow the development of complex structures and microenvironments, which means we lose out on a lot of the complexities of the tissues, while OoCs allow us to incorporate scaffolds and geometry to better simulate *in vivo* conditions.

For example, these figures show lung-on-a-chip, and we can see how it uses geometry and different cell types to completely simulate the blood-air-barrier found in the alveoli. And it is not hard to see how this is a much better way to study lung cells than flat 2D cultures.

And depending on the geometry and manufacturing methods, we can simulate the brain, liver, intestines, heart, eye… , basically any organ in the human body.

And if we combine all of them and add a circulatory system, we can simulate an entire human body.

For example, we want to test an oral drug, we can just inject the drug into the intestine-on-a-chip,

then it can go through all the organs like in the human body, from metabolism to excretion.

This allows researchers to directly model the pharmacokinetics and pharmacodynamics of the drugs very easily.

You might be wondering why we can't just use a mouse as a real *in vivo* model if we want to investigate the drug's interaction with every organ. The problem is that other animals are just other animals, and they are different from humans. And the predictive power is limited.

For example, an ebola vaccine was tested effective in other primates but it induced 10 times fewer antibodies in humans.

Another example of an HIV vaccine tested with other primates was found to actually increase the HIV risk for humans.

In general, the predictive power of animal trials can vary drastically.

Animal testing can also fail to detect toxicity of drugs.

In a case with an autoimmune antibody drug, it caused pulmonary embolisms and subsequent heart attacks in 2 out of 28 subjects because it unexpectedly binds to a platelet receptor specific to humans, and animal trials with monkeys could not detect this side effect.

If instead, the antibody drug was first tested using OoC, the researchers could have easily detected the toxicity of the drug, which could have not only drastically sped up drug development, but also prevented the death of the human test subjects.

Overall, the utility of OoC lies in it its predictive ability.

Compared to 2D techniques, it better simulates *in vivo* dynamics while not sacrificing the controllability. And compared to animal models, it gives higher predictive power while being cheaper and more ethical.

[Vincent]

Finally, I'll talk about future directions of this field.

Despite the advantages of LoC technology, there are still major obstacles to overcome.

For diagnostic applications as Helen introduced, the mass manufacturing of chips is still too complicated and expensive to be able to become true point-of-care devices.

And for the research applications as Ka introduced, although OoC testing is used to speed up drug development, the differences between it and human testing still need more validation data and still cannot completely replace it.