Biomarker is the measurable change associated with the disease [1]. It is easy to think that biomarkers appear as the disease develops. Most of studies followed the same suit. We like to see what changes when the disease is getting serious. It is OK when the starting point of the study is the clinical chief complaint. We can collect samples and measure what is changing as the disease develops. But how can we find changes earlier than the chief complaint or regular medical examinations? We want to move the starting point to an earlier time. After all the earlier diagnosis the better. It gives us the window for intervention before too late. Even if there is no current intervention available, it gives us the reference point to start searching for the ways to stop the disease. Some people will say we can work with animal models first. With animal models, we can collect samples even as early as the animal is born. We can find the earliest changes possible for that particular disease. I strongly support this strategy [2]. But what’s next? After we found the clues from the animal model, do we have to test them in clinical samples? At this validation stage, how do we find early cases before the chief complaint or regular medical examination? We can do prospective study. We can start to collect samples when everybody is healthy, until some of them are sick. This way, we solve all the problems.

But is it feasible or too expensive to collect that many samples from healthy people? At least it takes time for some of people to develop that particular disease. To finish a study in short time, it takes quite a large sample size.

Are there other ways of doing it?

We can make full use of this reversible equation.

Theoretically, we should be able to find the same biomarker making the opposite move when the disease is cured. The advantage of using this side of the equation is that it is much easier to identify patients with that disease than to identify healthy people who will develop the disease when they are still healthy. In this way, huge amount of resource will be saved. Compare to only a small fraction of samples are used in regular prospective studies, all the samples collected will be used. We finally have one example now [3]. It is good that people always asked me the same question when I suggested them to save urine samples by Urimeem, which is already a very cheap way. They always said that they can collect and preserve a lot of urine samples quickly, but how many of the samples will be used even if urimem is cheap. Answer can only be found when the right question is asked.

With the bottom part of the equation in mind, another idea came to me for solving the problem of no good animal models for some diseases. When there are many different kinds of effective drugs with different mechanisms for the same disease, they should all have a same desired curing effect and probably many different side effects too. With no animal model at all, may be we can test the effects of those drugs for this disease to see if there are common effects. Those common effects may then be tested in patients to see if they are really the biomarkers of the disease. No animal model is exactly the same as the human disease. Developing a new animal model is not easy. Some of the models are not easy to reproduce either. Compare to that, seeing the effect of different medications on animal is much simpler and easier.