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“Better future for cancer patients”

Cancer is one of the largest problems in this world. Millions of people are suffering from it, but there is no fundamental treatment. The problem might be based on current cancer researches. Most cases of them including anti-cancer drug screening are depending on cancer derived cell lines and their cancer gene mutations.

[Hypothesis & Test]
A Japanese cancer researcher artificially induced cancer on rabbits' ears by continuous inflammatory stimulation around 100 years ago. Cancer stem cells (CSCs) have recently been identified and currently considered to evoke cancer and its relapse. CSCs are believed to be resistant to chemo- and radio-therapies. Collectively, we raised a question, “Could chronic inflammatory environments induce CSCs?”

To evaluate this hypothesis, we used conditioned media derived from cancer cell lines mimicking chronic environment, because cancer cell lines often secrete inflammatory factors such as growth factors, cytokines and chemokines. Stem cells were treated with the conditioned media for 4 weeks to create CSCs without intended introduction of cancer-related gene or mutations. Thus, the created cancer stem cells (cCSCs) have always been assessed for their characteristics of self-renewal, pluripotency and tumorigenesis as well as drug resistances. We take these CSCs created by the effect of environmental conditions as the models of naturally developed cancer *in vivo*.
While different methods are found to establish CSCs, our method has a unique advantage that normal cells from not only cancer patients but also healthy people could be converted into cancer stem cells. The resultant cells would maintain the genetic background of any original cells.

[How cCSCs could be used]
Once cCSCs are established, they can be applied for the conventional analyses such as drug screening and gene comparison. Since the cCSCs keep gene backgrounds of donors, the data could be fed back to them directly. In this context, cCSCs can contribute to establish the strategy for “precision medicine” and “personalized medicine”. Even more, when the stem cells are provided from healthy people, we can convert them into cCSCs, which will be the model of CSCs reflecting the cancer that the donor might develop. This means the data might personally help diagnose themselves even in the future. This is the reason why we propose the development of the predictive treatment of cancer, to which the cCSCs can contribute.

[Current members and situation of LANFAM]
We are supported by the organizations of small and medium enterprises and the regional innovation. Our research currently depends on the facilities of Okayama University. LANFAM was established with our personal funds. Our representative director, Yoshio Shimizu, funded the most. He was impressed by the idea of cCSCs and aspired to establish a method to predict CSC development. I, Akimasa Seno, work here as a president and performs experiments in the technical advisor’s laboratory. I joined his group with some interests in his cCSCs idea. Since our technical advisor, Professor Masaharu Seno, will retire from Okayama University next year, his laboratory will be closed and will not be supported by the university. We are looking for a new research place.

[Our scenario of using cCSCs and current collaborators]
We are now just continuing to create cancer stem cells and research on them, focusing on how we can induce cCSCs. Researchers in Wayne State University in the US already have some interests in our cCSCs and already started collaborative studies with us. COSMO BIO Co., Ltd. is now planning to distribute our cCSCs. The cCSCs market is limited to a small number of researchers in the current

stage. Once it has got started to be provided, the importance will be spread to be known much more than ever before. We believe the market can be expanded to serve all people, not only researchers but also the others including both patients and healthy people, who are interested in their own CSCs. We are now looking for collaborators, funds and places to continue our work. Also, we are looking for stem cell providers, cCSC distributors, and other business partners. We do hope that the accumulated data with our cCSCs will be used for cancer predictions of all people.

[Q & A]
Q1.
cCSCs keep the original genomic background and there is no gene modification. The question is, “Is it your original idea?” Or “Is there any people or group in the world who are trying to create the cCSCs?”
A1.
The idea of cCSC is a very unique idea of Prof. Masaharu Seno who is our technical adviser, and no one other than our collaborators is trying to create cCSC yet. Since it takes at least 3 weeks to establish one cCSC line, we have to take so much care of the cells for successful results. Although this technique is not so much difficult, not so many people are able to handle the cells with concentrated care.

Q2.
I suppose the concept is used to screen drugs or other things. Are you going to take blood and analyze serum or something? Is that the approach? I think there was a slide showing that you're going to screen drugs.
A2.
I meant our cCSCs could be applicable for conventional analyses and purposes. Drug screening is one of them, which we will perform with established cCSCs. If you want to screen drugs with your own cells, you have to provide us some stem cells and we’ll convert them into cCSCs. The use of blood other than blood transfusion is currently prohibited in Japan by law.

Q3.
It would be much easier for pharma companies to collaborate with you if you can identify a certain molecule that makes cCSCs.
A3.
Yes, exactly. We are analyzing that at the same time, and we are now finding some molecules which can induce cCSCs.

Q4-1.
After the two mentoring sessions, the presentation itself was drastically improved very much. But still, of course, I must make some comments. I want to ask you to see the real market. Cancer market is very huge, but the marketing size of your products will probably be 0.1 percent or less than that. I cannot help asking how many other people or how many industries are involved to this end. You need to explain how you can contribute to a pharma in their drug discovery process. You will have to translate your research result into the proposition with business value. To accomplish this successfully, I think you will also need some partners to have those kinds of discussion many, many, many times, like, tens, or hundreds. All kind of the meetings will be necessary. And at the same time, I really strongly appreciate if you can propose a specific type of cancer to focus on. Starting analyses on a specific type of cancer, I think there will be more people who can share more questions on the availability of cCSCs in the same field. Then, the pharmaceutical company can make some proposal to them, even for the basic studies at least. At the beginning they are already segregated into the area of some specific types of cancer. It's up to you to decide which part of the pharmaceutical

companies to tie up with. It'll be really appreciated if you can make a little more effort to decide where to start.

A4-1.

We are still looking for such a partner who can discuss with those problems. But I know there are so many small cancer markets and most of them are not focusing on cancer stem cells and many researchers are focusing on cancers developed in specific organs. However, I believe that problems in cancer treatment wouldn't be solved if we only continue to focus on cancers separated into their organs as most of the cancer scientist have done up to now. I must tell you that cancer could be classified into 6 types regardless of organ; adenocarcinoma, squamous cell carcinoma, sarcoma, leukemia and lymphoma including myeloma and glioma. Our cCSCs could be differentiated into every type of those cells if we use pluripotent stem cells from the beginning. It means there should be no gap among organs. Our final aim is to establish fundamental treatment of all types of cancer, not organ specific. On the other hand, we can provide organ specific cCSCs also when we use organ derived stem cells and/or organ specific microenvironment. The demand should be depending on customers but not on us, suppliers. We will be just ready to follow the customers' choice.

Q4-2.

No, you must decide it. And of course, you must understand the type of cancer and cancer stem cell itself is merely a concept. Because cancer stem cell is still controversial, some people will immediately doubt and not try to use cCSCs even you start to deal with cancer stem cells. Therefore, you must be careful to choose your words to appeal. I have many things to think about.

A4-2.

Even though there're a lot of people who do not believe in cancer stem cells, cancer stem cells are truly existing and it could be a cancer treatment target. I must feel nothing have been done at pharma sides and we have to keep explaining how it is important until the information on the importance of CSCs is sufficiently shared. Moreover, some companies have successfully been establishing patient derived cancer stem cells regardless with their origins. There will be no doubt on our cCSCs to be commercialized as business if both classified phenotypes and tissue specific phenotypes have been focused.