

Trend-Setting Women Scientists of Biomedical Research in Japan

Sachi Sri Kantha¹⁾, Saori Yamamoto²⁾

ABSTRACT

Objective: In the aftermath of Haruko Obokata's flawed research on the so-called Stimulus Triggered Acquisition of Pluripotency (STAP) cells in 2014, we highlight the need for trend-setting women scientists of biomedical research in Japan.

Methods: Our focus was on identifying trend-setting women scientists of biomedical research in Japan, who did establish solid reputation, prior to Dr. Obokata. The names of such pioneer scientists were identified by tracking their landmark publications in biomedical journals.

Results: We could identify five women scientists whose contributions were trend-setting. These include, Kimiko Anno (1910-2009), Teruko Ishizaka (b. 1926), Tsuneko Okazaki (b. 1933), Tomoko Ohta (b. 1933) and Reiko Kuroda (b. 1947). Flawed research of Dr. Obokata and her medically-trained mentors (Niwa, Sasai and Vacanti) also emphasizes the need for inter-disciplinary education among biomedical graduates.

Conclusion: The lack of women biomedical scientists in Japan who had received international reputation is pitiable. Many causes (such as cultural 'stereotypes' of women in Asian countries, discriminatory education policies adopted by the past governmental authorities, unassertiveness among women politicians, and lack of ideal role models) can be attributed to this lack.

KEY WORDS

Kimiko Anno, Teruko Ishizaka, Tsuneko Okazaki, Tomoko Ohta, Reiko Kuroda, women scientists

INTRODUCTION

In a recent editorial published in this journal, Ekblad *et al.*¹⁾ focused on the need for inter-professional and intercultural training of medical students. In addition, we also recognize a vital need for inter-disciplinary education at the graduate medical schools in Japan.

Recent fiasco of the two highly touted publications of Haruko Obokata *et al.*^{2,3)} on Stimulus Triggered Acquisition of Pluripotency (STAP) cells in the *Nature* journal of January 30, 2014, emphasizes the need for such inter-disciplinary education among young graduate students in Japan. The results reported by Obokata's team in producing pluripotent stem cells from somatic cells by a convenient and simple low pH treatment^{4,5)} could not be reproduced by other researchers and raised serious doubts on the validity of STAP cells^{6,7)}. Despite a valiant defense offered by Obokata on her reported protocol⁸⁾, her two papers were retracted by the *Nature* on July 3, 2014 and her televised press conference came under ridicule⁹⁻¹³⁾.

Haruko Obokata's pathetic plight appears to be a good case study on lack of visibility of trendy women biomedical scientists in Japan. She became a 'media darling' for a short while in early 2014. Due to her gender, smiling face, youthfulness, fashion statement of altering interior lab décor with Moomin cartoon characters, and the habit of wearing a cooking apron (*kappogi*) gifted by her grandma in the lab, mass media in Japan promoted Obokata as a '*rikei joshi (rikejo)*' [loosely translated as 'spirited woman of science']¹⁴⁾. Her 'STAP cell' discovery was hyped as a potential finding of 'Nobel prize caliber' in regenerative medicine. Even an interview by Ryoji Noyori, the President of RIKEN and a 2001 Nobel laureate in chemistry, given to the *Japan News by Yomiuri*

Shimbun, in the post-publication of the two publications in the *Nature* journal, enhanced such a media attention¹⁵⁾. In this interview published on March 2, 2014 (before Obokata's work was adjudicated as fraudulent), Noyori praised Obokata as follows: "Obokata challenged herself. She has a very flexible mentality. Her talents and capability were inspired by exposure to many different kinds of people. I think RIKEN is the fourth place she has worked."

To counterbalance the young Obokata's dubious record in research, in this editorial, we pay a short tribute to five trend-setting women biomedical scientists of Japan. They did achieve international reputation and were in fact authentic '*rikejo*' of their times. Unlike Obokata, these five women biomedical scientists of Japan didn't suffer from media frenzy, when they published their un-adulterated discoveries or new ideas.

METHODS

By scanning the databases of biomedical publications such as PubMed and Web of Science, we identified the names and contributions of trend-setting women scientists in biomedical research in Japan, who had established a solid reputation, prior to Dr. Obokata.

RESULTS

Five pioneer women biomedical scientists of Japan with internation-

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1) Center for General Education, Gifu University

1-1 Yanagido, Gifu City 501-1193, Japan

2) Laboratory of Animal Production, Faculty of Applied Biological Sciences, Gifu University

1-1 Yanagido, Gifu City 501-1193, Japan

Correspondence to: Sachi Sri Kantha

(e-mail: srikanth@gifu-u.ac.jp)

al reputation were identified. All five were born in the first half of the 20th century. Their scientific achievements are summarized below, in chronological order of their birth.

Dr. Kimiko Anno (1910-2009), a glycobiologist, who had a life span of almost a century.¹⁶⁾ Between 1950 and 1953, Ms. Anno received graduate training under Melville Laurence Wolfrom (1900-1969) at the Ohio State University, and returned to Ochanomizu University. At this university, she established a strong glycobiology group, studying mucopolysaccharides and chondroitin sulfates present in various animals.^{17,18)}

Dr. Teruko Ishizaka (b. Sept.28, 1926), an immunologist and allergy specialist. In collaboration with her husband Dr. Kimishige Ishizaka (b. Dec.3, 1925), she gained her reputation for the discovery of immunoglobulin E (IgE) antibody. Ishizaka couple moved to USA in 1957, and were affiliated with University of Colorado School of Medicine, and subsequently at the Johns Hopkins University, Baltimore, Maryland. The discovery of IgE was first reported by Ishizaka team¹⁹⁾ in 1966, when they were at the Children's Asthma Research Institute in Denver. Next year marks the 50th anniversary of this celebrated discovery. A publication search in PubMed database indicates that between 1953 and 2013, in a career span of 60 years, Ishizakas have a cumulative total of 119 publications. This is quite a record, for a husband-wife team^{20,21)}. For the 1966 discovery of IgE, Teruko Ishizaka and her husband Kimishige Ishizaka received numerous international awards such as Passano Foundation Award (1972), Gairdner Foundation International Award, Canada (1973) and Borden Award (1979)²²⁾.

Tsuneko Okazaki (b. June 7, 1933), was a molecular biologist, affiliated to the Nagoya University. Akin to the Ishizaka couple, Tsuneko Okazaki and her husband Reiji Okazaki (1930-1975) worked as a group and became recognized for their 1968 hypothesis of discontinuous DNA replication and the role of Okazaki fragments in DNA replication.^{23,24)}

Tomoko Ohta (b. 1933) is a geneticist, affiliated with the National Institute of Genetics, Mishima^{25,26)}. She is a protégé of Motoo Kimura (1924-1994), population geneticist and the proponent of neutral theory of molecular evolution²⁷⁾. Ohta's claim to scientific recognition was her revised formulation which later was tagged as 'nearly neutral theory of evolution'.^{28,29)}

Reiko Kuroda (b. Oct. 7, 1947) is a biological chemist, affiliated to the University of Tokyo (previously) and currently at the Tokyo University of Science. Dr. Kuroda's speciality is on chirality (left-right handedness) in animals and chemical molecules^{30,31)}. Her research studies also have a medical dimension in the etiology of degenerative diseases like Alzheimer's Disease and diabetes mellitus type II³²⁾.

DISCUSSION

A good example for the need for inter-disciplinary education among medical graduates became visible in the Obokata's STAP paper³⁾. Not only Obokata (who received a PhD from Waseda University), even her mentors and co-authors Hitoshi Niwa (an MD degree holder), Yoshiki Sasai (an MD degree holder) and Charles Vacanti (an MD degree holder) had goofed in preparing the abstract of this retracted paper. Within days of the publication of the Obokata's STAP paper³⁾, one of us (S.S.K) submitted the following criticism to the correspondence section of the *Nature*, on Feb.1, 2014.

"The article titled, 'Stimulus-triggered fate conversion of somatic cells into pluripotency (H. Obokata *et al.* *Nature*, 505, 641-647, 2014) had generated much enthusiasm in the Japanese media, because the first author is a photogenic young woman scientist. In the abstract, phrases 'mammalian somatic cells' and 'mammalian cells' have been presented. But the main research model reported was mice. I'm not sure whether Obokata *et al.* had tried this method in other mammalian models? But, Austin Smith in his commentary in the same issue, do mention that 'they did not test other species'. If this was correct indeed, then zoologically-speaking the use of 'mammalian cells' is a bit of an exaggeration and should not be used in such reports as a generic term."

Unfortunately, this criticism was rejected for publication in the print edition of the *Nature*, 6 days later, for "limited space" reasons. By convention, the abstract of a research paper should provide the *exact details of what is presented in the study, and should not exaggerate the findings*. If Obokata *et al.*³⁾ had carried out the study in mice cells, they should have reported in the abstract that the study was done in mice cells, and omitted using the 'mammalian' word. This is because, whereas 'mammalia' is a class of vertebrates, 'mice' is a single animal representative of the mammalian class. One can infer that both Obokata and her medically-trained mentors (Niwa, Sasai and Vacanti) who guided her

research paper to get it published in the *Nature*⁸⁾, were inter-disciplinarily challenged to distinguish the difference between zoologically definable categories 'mice' and 'mammal'. We reiterate that this criticism is not nit-picking on the specific usage of words. Hence, our plea for the need for inter-disciplinary training for medical graduates. We believe that Obokata's scientific studies suffered badly due to lax guidance offered by her four mentors (above mentioned three, plus Teruhiko Wakayama). It is rather unbelievable that Obokata could gain such a skill to deceive not one, but four of her mentors who have had a higher publication record than her.

The lack of women biomedical scientists in Japan who had received international reputation is pitiable. Many causes can be attributed to this lack. These include, cultural 'stereotypes' of women in Asian countries, discriminatory education policies adopted by the past governmental authorities, unassertiveness among women politicians, and lack of ideal role models. The plight of current generation of women scientists in Japan as well as their career goals and potentials have occasionally received attention previously³³⁻³⁵⁾. According to an embarrassing statistic provided by Normille³³⁾, Japanese women made up only 11.1% of the scientific work force in 2004, whereas the corresponding figure in USA was 26%. The five trend-setting Japanese biomedical scientists we have highlighted here are only a representative sample. There should be many like these five, which we had excluded. An in-depth study on other women biomedical scientists is needed in the future.

As of now, 11 women scientists have been awarded the Nobel Prize in medicine or physiology. These include, Gerty Theresa Cori (1947), Rosalyn Yalow (1977), Barbara McClintock (1983), Rita Levi Montalcini (1986), Gertrude Elion (1988), Christian Nusslein-Volhard (1995), Linda Buck (2004), Françoise Barre-Sinoussi (2008), Elizabeth Blackburn (2009), Carol Greider (2009) and May-Britt Moser (2014). We earnestly hope for the day when a woman biomedical scientist from either Japan or from the Eastern hemisphere joining this elite group.

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