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PRESS RELEASE

関西医科大学
KANSAI MEDICAL UNIVERSITY

New research reveals the mechanism of regress for pigmented nevus. This research was published in "PLOS ONE" on November 1st.

Naoki Morimoto, an associate professor of the Department of Plastic and Reconstructive Surgery at Kansai Medical University, and his colleagues have revealed the mechanism of regress of pigmented nevi.

Pigmented nevi are black because of pigments called *melanin*. Although melanins are unable to exist in vivo for a long time, a pigmented nevus is able to remain part of an organism because nevus cells help sustain it.

Morimoto and his colleagues hypothesized that if nevus cells are destroyed, melanin will be absorbed into the body and the pigmented nevus will disappear.

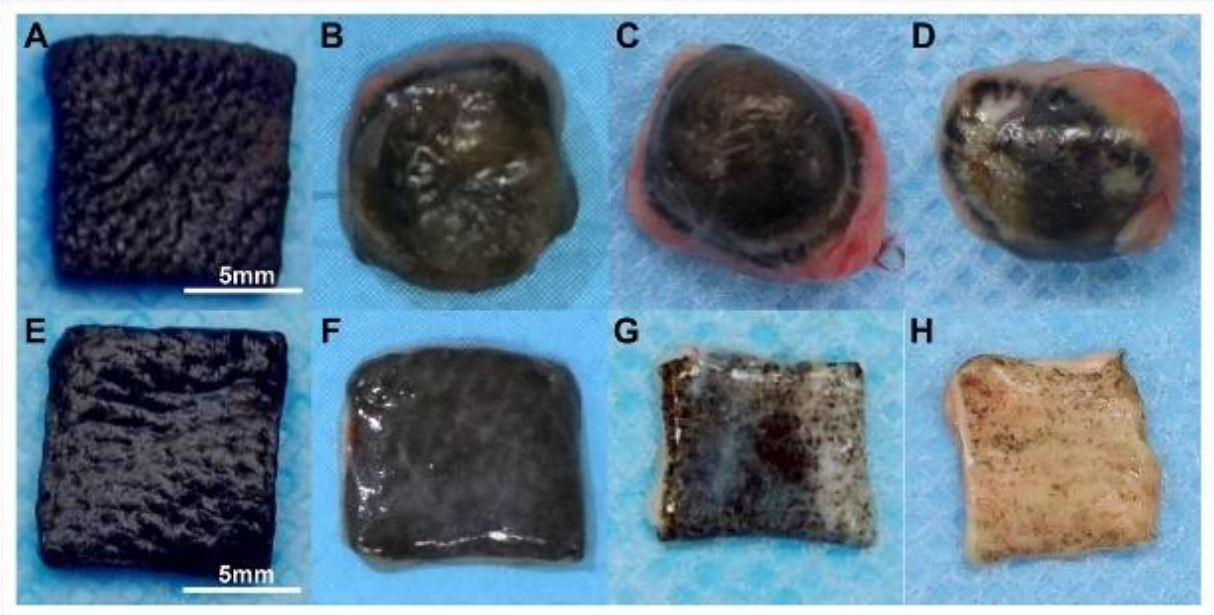
Morimoto and his colleagues performed a long-term observation of the color change of inactivated nevus tissue after high hydrostatic pressurization (HHP). Pressurized nevus specimens and non-pressurized nevus tissues were implanted subcutaneously in nude mice and then harvested 3, 6, and 12 months later. Color changes of the nevus specimens were evaluated. In the 200 MPa group, specimen color gradually regressed, eventually turning white, and brightness values were significantly higher than in the control group after 6 months. This indicated that melanin in the pressurized nevus tissue had spontaneously degraded and regressed.

This study demonstrated that when the nevus cells are destroyed, melanins are degraded and nevi regress spontaneously.

The findings of this study were published in "PLOS ONE" (a peer-reviewed open access scientific journal) at 4:00pm (EDT) on November 1st 2017.

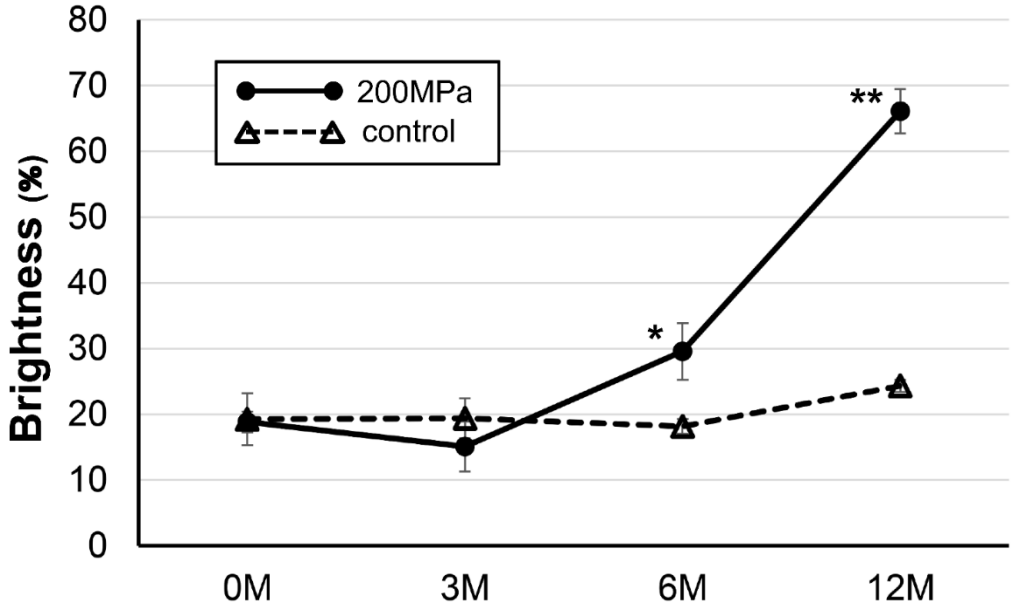
■Outline of the Article	
Title of the Journal	PLOS ONE. 10.1371/journal.pone.0186958
Title of the Article	Melanin pigments in the melanocytic nevus regress spontaneously after inactivation by high hydrostatic pressure
Authors	The Department of Plastic and Reconstructive Surgery at Kansai Medical University Morimoto Naoki - corresponding author, Kusumoto Kenji. The Department of Biomedical Engineering of National Cerebral and Cardiovascular Center Research Institute Yamaoka Tetsuji, Mahara Atsushi. The Department of Plastic and Reconstructive Surgery, the Graduate School of Medicine Kyoto University Suzuki Shigehiko, Jinno Chizuru, Sakamoto Michiharu, Ogino Syuichi.

Since 2016, Morimoto and his colleagues have carried out ten clinical trials on patients with congenital melanocytic nevi. To apply for Advanced Medical Care B as defined by the Ministry of Health, Labour and Welfare, the team is now preparing five more clinical trials based on the results of this latest study.



■Photographs of the nevus specimens before implantation, at 3 months, 6 months, and 12 months for the control and 200 MPa groups.

Top：non-pressurized nevus tissues A：before implant B：3 months C：6 months D：12 months
Bottom：pressurized nevus specimens E：before implant F：3 months G：6 months H ：12 months



■The mean brightness values of nevus specimens for the control and 200 MPa groups.
The brightness values at 6 and 12 months are significantly higher in the 200 MPa group than in the control group.

Appendix

[Method of the study]

Long-term observation of the color change of inactivated nevus tissue following HHP. Pressurized nevus tissues (200 MPa group, n = 9) and non-pressurized nevus tissues (control group, n = 9) were implanted subcutaneously in nude mice (BALB/c-nu) and then harvested 3, 6, and 12 months later.

The findings of this study were published in “PLOS ONE”, a peer-reviewed open access scientific journal, on November 1st 2017.

[High hydrostatic pressurization; inactivation of nevus tissue]

Collaborators of this study, Professor Fujisato at Osaka Institute of Technology and Dr. Yamaoka – director of the Department of Biomedical Engineering of National Cerebral and Cardiovascular Center Research Institute – developed a technique to remove nevus tissue using HHP. High-pressure treatment has been a popular research tool in areas like food processing and it has been proven safe. For example, treating an egg at 700 MPa for 10 minutes causes the egg to congeal because of protein denaturation. 700 MPa corresponds to approximately 7 times the ocean bottom pressure at Mariana Trench.

When an egg is given high-pressure treatment in physiological saline, the egg does not crack because water does not compress much.

High-pressure treatment is expected to be a good disinfection method because bacteria and viruses are destroyed at > 607MPa.

In this study, Morimoto and his colleagues processed nevus tissue at 200 MPa for 10 minutes. This HHP treatment successfully deactivated nevus without damaging the collagen that forms the basis of the dermis.

Previous studies have shown that all kinds of cells in human skin, porcine skin, and nevus tissue were completely inactivated after HHP at >200 MPa for 10 minutes. Furthermore, the cultured epidermis survived on the skin and nevus inactivated by HHP.

[Background]

The leader of this study was Naoki Morimoto, an associate professor of the Department of Plastic and Reconstructive Surgery at Kansai Medical University.

The Department of Biomedical Engineering of National Cerebral and Cardiovascular Center Research Institute, the Department of Plastic and Reconstructive Surgery, the Graduate School of Medicine of Kyoto University and Osaka Institute of Technology were involved as collaborative partners.

Moreover, this study was supported by Practical Research for Innovative Cancer Control of AMED, the Japan Agency for Medical Research and Development, founded on April 1st 2016.

The previous study completed the clinical trials and case registration as clinical research class 2 as defined by the Act on the Safety of Regenerative Medicine came into force on November 25th, 2014.

To apply for Advanced Medical Care B as defined by the Ministry of Health, Labour and Welfare, the team is now preparing five more clinical trials based on the results of this latest study.

【For inquiries about this press release】
Kansai Medical University
Public Relations Office (Okada, Hatamori, Sawaki, Oshiro)
2-5-1 Shin-machi, Hirakata City, Osaka 573-1010 Japan
TEL：+81-72-804-2128　FAX：+81-72-804-2547　email：kmuinfo@hirakata.kmu.ac.jp

Naoki Morimoto, Associate Professor of the Department of Plastic and Reconstructive Surgery
TEL：+81-72-804-0101　FAX：+81-72-804-2031　email：morimotn@hirakata.kmu.ac.jp

【For inquiries about general cancer control】
Ministry of Health, Labour and Welfare
Cancer and Disease Control Division, Health Service Bureau
1-2-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-8916 Japan
+81-3-5253-1111

【For inquiries about Practical Research for Innovative Cancer Control】
Japan Agency for Medical Research and Development
Division of Cancer Research, Department of Research Promotion
20F Yomiuri Shimbun Bldg. 1-7-1 Otemachi, Chiyoda-ku, Tokyo 100-0004 Japan
TEL：+81-3-6870-2221　FAX：+81-3-6870-2244　email：cancer@amed.go.jp