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研究課題名(和文) Incontinence-associated dermatitis by infected urine: biological mechanisms and prevention strategies

研究課題名(英文) Incontinence-associated dermatitis by infected urine: biological mechanisms and prevention strategies

研究代表者

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交付決定額(研究期間全体)：(直接経費) 2,200,000円

研究成果の概要(和文)：My research with this JSPS grant aimed at understanding the mechanisms of incontinence-associated dermatitis (IAD) induced by urine and bacteria. In the first year, my research showed that after a specific time point urine promotes the growth of bacteria.

研究成果の学術的意義や社会的意義

My research findings are important for the development of new innovative prevention/treatment strategies for IAD. The animal model I have established can serve as the basis for future studies to test the effectiveness of novel strategies to prevent the development of IAD.

研究成果の概要(英文)：Therefore, in the next step I wanted to develop a novel animal model for IAD by combing urine and bacteria. My studies showed that bacteria on damaged skin, have the ability to invade the epidermis and this induces IAD which is characterized by skin barrier disruption, inflammation and persistent redness. I have presented my research findings at national and international conferences and received the Young Investigator award by the Japanese Society for Wound Healing.

研究分野：Nursing Science

キーワード：IAD skin barrier incontinence older patients

1. 研究開始当初の背景 (background of the research)

Incontinence-associated dermatitis (IAD) is a painful inflammatory condition due to chronic exposure of skin to urine and/or feces. Current preventive measures are not sufficient, and as a result IAD is highly prevalent in older incontinent patients leading to reduced Quality of Life. This is a particular problem for Japan's rapidly aging society. In order to develop novel targeted prevention strategies, we need to understand the underlying mechanisms.

2. 研究の目的 (the purpose of the research)

In patients with urinary incontinence, prolonged exposure to urine only leads to maceration and its pH is not damaging on healthy skin (Koudounas et al., 2022). However, malodorous urine, due to the presence of bacteria, has been identified as a risk factor for IAD (Ichikawa-Shigeta et al., 2014). Therefore, in this research I aimed to investigate and reveal the histopathological mechanisms by which urine and bacteria lead to IAD.

3. 研究の方法 (the method of the research)

Prof Sanada's research group, at the University of Tokyo, have recently explored the mechanisms of IAD caused by liquid stool (Mugita et al., 2015). In particular, they have shown that exposure to digestive enzymes in liquid stool impairs skin barrier function, evident as maceration, and facilitates the invasion of bacteria to the dermis, leading to tissue damage and inflammation (Figure 2). To address the research purpose, I used Sprague Dawley (SD) rats to establish an IAD model induced by urine and bacteria. To simulate skin maceration by urine, synthetic human urine (s-urine) was applied topically on the dorsal skin of rats using agarose gels, and subsequently inoculated with *Pseudomonas aeruginosa*, commonly found in the perineal skin of incontinent patients. To assess skin barrier function, measurements of transepidermal water loss and skin pH were obtained. Skin appearance and histopathological features were assessed macroscopically and by histology, respectively, to reveal the changes in skin tissue structure in response to urine and bacteria.

4. 研究成果 (the achievement of the research)

During the first year of my research, I examined the effects of urine on bacterial proliferation, which is a key component of IAD pathogenesis. I focused on bacterial species commonly found in human urine, including *P. aeruginosa*, *Proteus mirabilis*, *E. Coli* and *Klebsiella pneumoniae*. My findings revealed that s-urine, has an inhibitory effect during the early phase of growth (0-6 hrs), but with increasing time (≥ 8 hrs) the inhibitory activity of urine decreases and promotes bacterial growth (Figure 1).

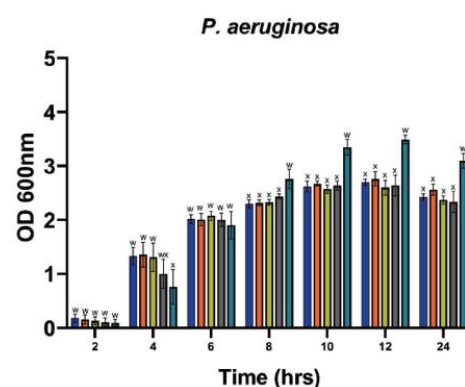


Figure 1. Bacterial growth during cultivation with s-urine.

Following these findings, last year I successfully developed a novel model of IAD due to the combined exposure to urine and *P. aeruginosa*. This clinically relevant model fulfills the clinical criteria of IAD including persistent redness, skin barrier disruption, inflammation and infection. This model is very promising and may be used in future studies to develop new prevention strategies for IAD.

My work has been presented in national and international conferences, including the Japanese Society for Wound Healing (JSWH) and the 9th Asia Pacific Enterostomal Therapy Nurse Association Conference. During the 51st JSWH conference I also received the Young Investigator Award. My research has also been disseminated in the form of three peer-reviewed first-author articles in national and international journals.

5. 主な発表論文等

〔雑誌論文〕 計2件（うち査読付論文 2件/うち国際共著 2件/うちオープンアクセス 2件）

1. 著者名 Sofoklis Koudounas, Yuko Mugita, Takeo Minematsu, Gojiro Nakagami, Carolina Weller, Hiromi Sanada	4. 巻 30
2. 論文標題 Does the presence of bacterial urinary infection contribute to the development of incontinence-associated dermatitis? A scoping review	5. 発行年 2021年
3. 雑誌名 Journal of Tissue Viability	6. 最初と最後の頁 256-261
掲載論文のDOI（デジタルオブジェクト識別子） 10.1016/j.jtv.2021.01.008	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1. 著者名 Sofoklis Koudounas, Takeo Minematsu, Yuko Mugita, Ayano Nakai, Hiromi Tobe, Chihiro Takizawa, Mao Kunimitsu, Gojiro Nakagami, Hiromi Sanada	4. 巻 -
2. 論文標題 Bacterial invasion into the epidermis of rats with SLS-irritated skin increases damage and induces incontinence-associated dermatitis	5. 発行年 2022年
3. 雑誌名 International Wound Journal	6. 最初と最後の頁 -
掲載論文のDOI（デジタルオブジェクト識別子） なし	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

〔学会発表〕 計2件（うち招待講演 0件/うち国際学会 0件）

1. 発表者名 Sofoklis Koudounas, Takeo Minematsu, Gojiro Nakagami, Yuko Mugita, Sanai Tomida, Hiromi Sanada
2. 発表標題 Development of an in vitro model of urinary infections to study the mechanisms leading to incontinence-associated dermatitis in patients with urinary incontinence
3. 学会等名 8th conference of the Japanese Society for Nursing Science and Engineering
4. 発表年 2020年

1. 発表者名 Sofoklis Koudounas, Yuko Mugita, Takeo Minematsu, Gojiro Nakagami, Sanai Tomida, Hiromi Sanada
2. 発表標題 The effects of urine on bacterial growth and motility: Implications in the development of incontinence-associated dermatitis
3. 学会等名 49th Japanese Society for Wound Healing
4. 発表年 2019年

〔図書〕 計0件

〔産業財産権〕

〔その他〕

Department of Skincare Science http://skincarescience.m.u-tokyo.ac.jp Global Nursing Research Center http://gnrc.m.u-tokyo.ac.jp/ Global Nursing Research Center, Univ Tokyo http://gnrc.m.u-tokyo.ac.jp/

6. 研究組織

	氏名 (ローマ字氏名) (研究者番号)	所属研究機関・部局・職 (機関番号)	備考
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7. 科研費を使用して開催した国際研究集会

〔国際研究集会〕 計0件

8. 本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関
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