

## ABSTRACT OF DISSERTATION

Title	Dendritic Cells Directly Recognize Nickel Ions as an Antigen during the Development of Nickel Allergy (樹状細胞はニッケルアレルギーの発症時にニッケルイオンを抗原として直接認識する)
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<p><b>【Introduction】</b> Metal hypersensitivity is a disorder of the immune system, usually manifested as an allergy to metals in daily contact. It is a public health problem that brings heavy physical, mental and economic burdens to patients. The molecular mechanism by which metals enter the human body and cause allergic diseases is still elusive. It is believed that the eluted metal ions are captured by dendritic cells (DCs) and transferred to draining lymph nodes to activate T cells.</p> <p><b>【Purpose】</b> The purpose of this study was to further clarify the initial mechanism of metal allergy, that is, the extent to which invading metal ions are carried in DCs, how they react with keratinocytes, and how they spread.</p> <p><b>【Method】</b> <i>In vitro</i>, we used a metal indicator, Newport Green Newport Green™ DCF, to locate the most common allergenic metal, nickel (Ni) ions, in the bone marrow-derived DCs (BMDCs) stimulated with 25 μM NiCl<sub>2</sub> at different time periods. <i>In vivo</i>, we used a Ni allergy mouse model, and confirmed the location of Ni ions in the epidermal DCs and draining lymph nodes over time.</p> <p><b>【Results】</b> Ni ions entered BMDCs and showed positive staining in keratinocytes <i>in vitro</i>. Capturing Ni ions did not affect the activity of DCs. A time varied quantitative analysis <i>in vivo</i> demonstrated that at 1 hour, a small amount of Ni ions was observed in the epidermis. After 6 hours, the number of Ni ions that entered the epidermal sheet reached a peak and remained constant for a few days, gradually emitted 48 hours later. In the cervical lymph nodes of mice, accumulation of Ni ions reached a peak within 24 hours</p>	

and then gradually decreased.

**【Conclusion】**

In our study, we used Newport Green, a metal indicator, to visually prove that Ni ions can be indeed captured by DCs, and Ni ions are transferred from epidermis to draining lymph nodes over time. The findings of this study will contribute to the development of effective diagnoses and treatment methods for patients allergic to Ni.