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## Press release

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# Buruli Ulcer: Mechanism Behind Tissue Erosion Revealed

Scientists at the Pasteur Institute in Paris and the CNRS (French National Center for Scientific Research), in collaboration with the Universities of Basel (Switzerland) and Cambridge (UK) have identified the mechanism underlying the formation of Buruli ulcers caused by the bacterium *Mycobacterium ulcerans*. Their discovery opens avenues for the development of novel therapeutic approaches for combating this disfiguring skin disease. This study is published online by *The Journal of Clinical Investigation*.

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Buruli ulcer is a cutaneous tropical disease caused by the bacterium *Mycobacterium ulcerans*. These bacteria are believed to be inoculated by biting insects into the skin, where they multiply and induce the formation of chronic open sores, sometimes affecting entire limbs. Buruli ulcer is rarely fatal, but since the 1980s disease incidence has risen alarmingly in rural areas of West Africa, where it causes a heavy burden of disfigurement that can lead to ostracism.

The destruction of cutaneous tissue is due to a lipid toxin called mycolactone that is secreted by the bacilli. Now, thanks to research led by Caroline Demangel at the Pasteur Institute in Paris in collaboration with Marie-France Carlier at the CNRS in Gif-sur-Yvette (France), the molecular target and mechanism of action of this toxin have been identified.

Caroline Demangel's group together with collaborators at the Pasteur Institute and at the Universities of Basel and Cambridge have shown that mycolactone alters the architecture of epithelial cells by dysregulating the synthesis of their cytoskeleton, which is made of actin filaments. Cytoskeletal dynamics are essential in maintaining epidermal cell junctions, as well as the coordinated migration of cells towards sites of injury. By destabilizing the cytoskeleton, mycolactone therefore compromises both the integrity of cutaneous tissue and its potential to heal.

The current treatments for Buruli ulcer are based on intense antibiotic regimens, sometimes coupled with surgery to remove lesions, interventions that are poorly adapted to field conditions in regions where the disease is most prevalent. Blocking the ulcerative action of mycolactone could reduce current treatment regimes and eventually end them all together. The identification of the Wiskott-Aldrich syndrome proteins as molecular targets of mycolactone opens up original avenues of research towards the development of inhibitors that could provide alternative therapeutic options for the treatment of this disfiguring disease.

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## Source

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**Mycolactone activation of Wiskott-Aldrich syndrome proteins underpins Buruli ulcer formation**, *The Journal of Clinical Investigation*, March 15, 2013

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