

## Bridging Borders Through Science: Collaborative Efforts in Diabetic Limb Preservation between Cuba and the USA

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**Date of receipt: November 2024**

**Date of acceptance: November 2024**

### Abstract

The re-establishment of diplomatic relations between Cuba and the USA in 2014 has brought about a new era of medical collaboration. Limb preservation, particularly in patients with diabetes, represents a crucial area where bilateral efforts have yielded significant advances. This manuscript explores the historical and scientific collaboration between Cuban and American researchers in diabetic foot care, focusing on marrying interdisciplinary teams with technology, cell biology, and enhancing wound healing. These efforts have not only advanced diabetic limb preservation but also illustrate how scientific diplomacy can bridge geopolitical divides for the greater good of human health.

**Keywords:** *limb preservation, diabetic foot ulcers, egf therapy, international collaboration, scientific diplomacy*

### Context

On December 17, 2014, the Presidents of the United States and Cuba announced the reestablishment of diplomatic relations, opening new doors for cooperation in multiple fields, including healthcare. Diabetes and its complications have emerged as one of the most urgent public health crises, affecting millions worldwide. Among the most devastating complications are diabetic foot ulcers (DFUs), which precede 80% of lower extremity amputations globally. With more than 18.6 million people affected annually, DFUs present a significant healthcare challenge, particularly in underserved populations.

Limb preservation, a field aimed at reducing preventable amputations, has been a focal point for collaboration between Cuban and American researchers. The unique strengths of each nation—Cuba's emphasis on preventive, community-based care, and the USA's technological advances—have enabled the development of new therapies and protocols that address the multifaceted nature of diabetic foot disease. This manuscript explores the collaborative journey between researchers from both countries, focusing on key innovations in EGF therapy, oxidative stress management, and cellular mechanisms that underpin successful wound healing.

### Scope of the problem

DFUs represent not only a clinical challenge but a profound socioeconomic burden. Approximately 50% of ulcers become infected, with up to 20% of those cases leading to lower extremity amputations. The 5-year mortality rate for patients with DFUs is staggering, exceeding 30%, and rising to more than 70% in patients who undergo major amputations. The direct costs associated with treating DFUs in the USA alone are estimated to range between \$9 billion and \$13 billion annually. This significant burden highlights the urgent need for innovative, effective, and affordable interventions, a need that has driven the US-Cuba collaboration in diabetic limb preservation research.

### History and Initiation of the Collaboration

The US-Cuba partnership in limb preservation began long before the normalization of diplomatic relations in 2014. Discussions with colleagues at the Center for Genetic Engineering and Biotechnology (CIGB) in Cuba, where groundbreaking work in epidermal growth factor (EGF) therapy had already shown promise in accelerating wound healing led to an acknowledgement of the scope of the problem and the promise of collaboration.

Our initial meetings focused on the shared public health burden of diabetes and its complications. Cuba's well-established healthcare infrastructure, with its focus on community engagement and preventive medicine, was a natural complement to the USA's technological prowess in medical devices and wound care innovations. This partnership has since led to numerous joint publications and the exchange of scientific expertise across borders, laying the foundation for our ongoing research efforts. It has also led to numerous collaborative clinical visits between nations (Figures 1-4).

#### Key Advances in Limb Preservation Research

1. **Epidermal Growth Factor Therapy:** The use of EGF in diabetic wound healing has been one of the most promising contributions from Cuba to this collaborative effort. EGF promotes cell proliferation, migration, and differentiation—critical processes in tissue repair. Collaborative work, including “Healing enhancement of diabetic wounds by locally infiltrated epidermal growth factor,” demonstrated that regional infiltration of EGF in diabetic foot ulcers not only accelerates healing but also reduces systemic oxidative stress, a key contributor to chronic wounds in diabetes. This therapy has since been integrated into clinical protocols for wound care in both Cuba and the USA, offering a new avenue for improving outcomes in high-risk diabetic populations.
2. **Reduction of Oxidative Stress:** Oxidative stress is a well-known driver of cellular damage in chronic wounds, particularly in patients with diabetes. Through our collaborative research, we identified that locally administered EGF not only facilitated wound healing but also modulated systemic oxidative stress markers. This systemic benefit was a groundbreaking discovery, indicating that therapies targeting local wound environments could also positively impact overall metabolic health. Such findings are of significant importance in resource-limited settings, where reducing hospitalizations and long-term complications is critical.
3. **Cellular Mechanisms in Wound Healing:** One of the most challenging aspects of DFUs is the cellular dysfunction associated with diabetic tissue. Our work, including the study “Expression of cell proliferation cycle negative regulators in fibroblasts of an ischemic diabetic foot ulcer,” explored the cellular dynamics within diabetic wounds. Work led by my colleague Jorge Berlanga at CIGB found that fibroblasts from DFUs exhibit premature senescence and increased expression of cell cycle inhibitors such as p53 and p21. These molecular roadblocks prevent adequate tissue regeneration, resulting in chronic, non-healing wounds. This discovery has since influenced treatment approaches that target these molecular pathways to promote more effective healing.
4. **Integration of Multidisciplinary Care:** Multidisciplinary care is essential for reducing the risk of major amputations in patients with DFUs. Drawing on our experience from both nations, we have emphasized the importance of integrated care teams consisting of podiatrists, vascular surgeons, infectious disease specialists, and primary care clinicians. Our recent JAMA publication reinforces that this multidisciplinary approach reduces the risk of amputation and improves overall patient outcomes. The collaboration has also fostered training programs, where Cuban clinicians are exposed to the latest technological advancements in offloading devices, thermal imaging, and wound assessment tools developed in the USA.

### Challenges and Lessons Learned

While the collaboration between Cuban and American researchers has yielded significant results, it has not been without challenges. Geopolitical tensions, trade restrictions, and limited access to advanced medical tech-

nologies in Cuba have occasionally hampered the full realization of our research goals. However, these challenges have underscored the importance of scientific diplomacy as a tool for overcoming barriers. The perseverance of researchers on both sides has demonstrated that healthcare transcends borders, and that shared knowledge can bring about limb and life-saving innovations.

The COVID-19 pandemic, in particular, has highlighted the fragility of global scientific collaborations. Travel restrictions and resource reallocations disrupted some of our ongoing studies, particularly those involving in-person clinical trials. Nonetheless, the pandemic also reinforced the value of international partnerships in healthcare research, as virtual collaborations and data-sharing platforms emerged to sustain momentum in our work.

## Conclusion

### The Future of US-Cuba Medical Cooperation:

The collaborative efforts between Cuba and the USA in diabetic limb preservation have set the stage for further medical partnerships. As we look to the future, there are opportunities to expand this collaboration into other areas of chronic disease management, such as cardiovascular health, renal disease, and neurodegenerative conditions. The success of EGF therapy and our joint research on oxidative stress and cellular dynamics in wound healing provide a template for future breakthroughs. Moreover, as the global burden of diabetes continues to rise, expanding access to these innovations in underserved regions will be critical.

Cuba's preventive healthcare system, which emphasizes community-based interventions and early detection of chronic diseases, could greatly benefit from integration with technological advancements from the USA. Collaborations could focus on population health management, leveraging health data analytics, telemedicine, and mobile health platforms to improve the detection, monitoring, and treatment of chronic diseases such as diabetes and cardiovascular diseases. This would also facilitate the development of cost-effective health strategies that could be implemented not only between Cuba and the USA but also in low- and middle-income countries (LMICs) facing similar challenges.

### The Role of Scientific Diplomacy

The US-Cuba partnership in limb preservation illustrates the power of scientific diplomacy. Despite the political challenges that have historically divided our nations, the collaboration has advanced not only healthcare outcomes but also diplomatic relations. The work we have done in limb preservation is not just a triumph of science; it is a demonstration of how two nations can come together for the shared goal of improving human health. This partnership serves as a model for other nations grappling with the dual burdens of chronic disease and limited healthcare resources.

As we continue to build on the foundation of this collaboration, it is imperative that we expand our efforts to include more stakeholders —government agencies, private sector companies, and international organizations— so that the innovations developed through this partnership can reach the people who need them most.

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Prof. Armstrong making rounds in Hospital Dermatológico Guillermo Fernández Hernández Baquero, Cuba, December 2012.



David G. Armstrong (right) being interviewed by Cuban National TV's Niurka Damarys following keynote at Cuban International Symposium on Diabetes and its Complications, 2016.



CIGB's Prof. Jorge Berlanga with Profs Marvin J. Slepian (middle) and David G. Armstrong following Cuban wound healing symposium, 2016.



Prof. Armstrong in Limb Preservation Clinic at University of Arizona with nurse Katherine Broze and Ambassador Jose Ramon Cabañas, 2016.