<u>Achievements for 2017- 2018:</u> US-Ireland- Northern Ireland R&D partnership between the NSF-ERC for Revolutionizing Metallic Biomaterials (ERC-RMB) in the US and CÚRAM at NUI Galway, Ireland, and NIBEC at Ulster University, Northern Ireland: NSF-SFI-C2C

Accomplished thus far with the C2C supplement

- Seven conference calls and webinars with technical presentations have occurred, with the entire C2C team, along with industrial partners OrthoKinetic, Inc, NC, USA and Ft. Wayne Metals (FWM) IN, USA, that focused on details of bioresorbable orthopedic implants made from novel high strength, high ductility magnesium and magnesium alloy systems that can replace the permanent metals/metal alloys usually used in applications ranging from thin wires (for clinical use as "k wires") to thicker pins, rods and elastic stable intramedullary nails (IMs or ESINs), as well as meshes for the treatment of complex bone fractures.
- Materials Transfer agreements, MOUs, NDAs have been signed among the C2C and Industry members.
- First set of key biodegradable magnesium alloy systems developed by the NSF-ERC-RMB using novel alloy processing methods (invention disclosures filed) have been shipped to NIBEC at Ulster University. Ulster has employed advanced surface modification and coating procedures to control key interfacial properties for our clinical applications.
- NCAT has finished preparation of a Mg materials data base from the ERC-RMB accomplishments and is in discussion with both academic and industrial members. A subset of mechanical properties of ERC-RMB alloys produced at NCAT and Pitt was provided to industrial team members and FEA specialists in Ireland to drive the testing and discussion of promising alloy candidates.
- New sets of Mg alloys are processed based on surgical requirements and specific dimensions provided by clinicians for bone nails surgery. The Mg alloy strength and stiffness requirements specific to pediatric patient are being developed given they can be lower to those of SS or Ti.
- In May-June 2018, new sets of alloys (including higher strength and stiffness LPSO system) will be developed and tested at UC medical center and will be shipped to Ireland for new coating shear studies and FEM modeling.
- Detailed finite element models have been developed at the Science Foundation Ireland Centre for Research in Medical Devices (CÚRAM) at the National University of Ireland, Galway (NUIG) that model 3-point bending tests for samples with and without corrosion and IM in-bone insertion.
- Clinicians from Ireland and the US have supplied surgical requirements for k-wires and IMs. Appropriate animal models are being explored in initial tests based on these requirements.
- Patrick Lemoine from Ulster University visited ERC-RMB during summer 2017.
- Jonathan and Stephen (UUlster Postdoc and PhD student) and Enda and Lizanne (NUI, Galway) will spend a day or two with each of the groups at NCAT, Pitt and UC. The visit is being planned for the last two weeks of June 2018 (18th-29th).
- ERC-RMB members at NCAT and UC have produced Mg alloy rods and wires through single crystal formation or thermomechanical extrusion for *in-vivo, in- vitro* experiments.
- Mg Intramedullary Bone nails (IMs), provided by ERC groups and industrial partner FWM, were tested for biomechanical properties (2017). All but one type of Mg IMs had sufficient strength to withstand insertion and extraction pressures, using pig cadaveric fore-leg bones.
- A 4-point bending protocol was refined, involving a UC bioengineering inter, to fulfill ASTM F1264 standards, with reduced support spacing for smaller specimens. It is hypothesized that the stiffness of Mg IM nails needed to be ~ 25-50% that of current IMs and testing of ERC-RMB materials is planned.

- Multiple types of surgical nails for C2C are being produced using single crystal technology and ERC-RMB magnesium alloys. Proprietary methods developed by ERC-RMB are being used to prepare surgical meshes made of magnesium.
- Dr. Pat McGarry (CÚRAM the SFI Centre for Research in Medical Devices (SFI), based at the National University of Ireland Galway), has hired personnel and they are working on the computational modeling of the bone and Mg materials.
- ERC-RMB-C2C will participate and present activities at the NSF-C2C workshop at UCLA, Aug 14-15, 2018.

Participants from USA:
USA only: Industry members (3), Faculty (5), Students (4 G, 3UG), Clinicians (2), Scientists: (4)

Quantifiable outputs that have been produced thus far

- Three (3) international keynote talks and one at the NSF-CREST national meeting by Dr Sankar in which C2C program and its activities were presented emphasizing its wisdom, vision and impacts.
- Based on NCAT activity a US provisional application has been filed and assigned U.S. Serial No. 62/665,921
- Joint paper published on Mg corrosion in vitro and in vivo through a collaboration between ERC researchers (UC, Pixley) and industrial members at Ft. Wayne (funded in part by C2C). Griebel, AJ, Schaffer, JE, Hopkins, TM, Alghalayini, A, Mkorombindo, T, Ojo, KO, Xu, Z, Little, KJ, Pixley, SK 2017. "An in vitro and in vivo characterization of fine WE43B magnesium wire with varied thermomechanical processing conditions". J Biomed Mater Res Part B 2015:00B:000–000. DOI: 10.1002/jbm.b.34008.
- Joint paper between UC and NCAT "Testing magnesium metal alloys for use as pediatric bone nails; K.Little, S.Pixley, D.Glos, V. Shanov and Z. Xu., European Cells and Materials Journal, Volume NN, ISSN 1473-2262

C2C research impact to revolutionize medical practice/treatment

Complex orthopedic fracture fixation in pediatric, young adult and baby boomers uses a range of stable bio-inert alloys such as Ti6Al4V. The limitations include the need for secondary surgery, especially in cases of high energy trauma in the young (traffic accidents, falls from height, sports injuries, etc.) and osteoporotic fractures in the elderly that lead to risks of inflammation and further fractures.

The C2C's bioresobable Mg alloys of high strength, high ductility in pins, wires, rods and elastic stable intramedullary nails can provide the solution as the next generation of improved devices offering significant therapeutic advantages over implants used today.

Modern industry is global and so should the training of our current and future researchers. The regulatory landscape, especially for biomedical materials and devices, is highly dependent on intercountry efforts. This tripartite partnership is creating a unique convergence of world-leading expertise from academia and industry in the fields of materials processing, surface characterization, and computational modeling with the shared goal of developing bioresorbable magnesium (Mg) alloy systems for orthopedic implant devices. As a global research team, we communicate person-to-person on the different challenges associated with each country's academic, industrial, and regulatory challenges.

In particular, the participation of Fort Wayne Metals with infrastructure in both the US and Ireland serves as a real-life mentor to the research team in these areas. The international and highly interactive nature of

this program empowers us to envision a unique next-generation workforce within the global knowledge economy. We plan to leverage this opportunity via student and faculty transatlantic visits and cross-institution offerings of seminars and lectures this year, as outlined in the program funding.

Improvement healing/treatment process for an individual and how C2C research revolutionizes medical practice/treatment

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