401 N. Lindbergh Blvd.
St. Louis, MO 63141
Tel.: 314.993.1700, #546
Toll Free: 800.424.2841, #546
Fax: 800.708.1364
Cell: 314.283.1983
Send via email to: jbode@aaortho.org and cyoung@aaortho.org

**AAO Foundation Final Report Form**
**(a/o 1/3/2018)**

Type of Award, Research Aid Award

Name(s) of Principal Investigator(s): Mohamed Nur Abdallah

Institution: University of Toronto

Title of Project: Use of a novel anabolic conjugate drug on a biomaterial for bone regeneration

Period of AAOF Support: 07-01-19 to 06-30-20

Amount of Funding: 4958 USD

## Summary/Abstract

The project aim was to provide a proof-of-concept for the local delivery of a novel bone forming drug using a synthetic biomaterial as a new therapy to repair and fill bone defects in patients with cleft lip and palate. Such treatments are crucial for filling the bone defects in order to stabilize the jaw, allow tooth eruption and facilitate the placement of dental implants to replace missing teeth. This work produced from this project was published in two articles published in peer-reviewed journals.

- **Abstracts of published articles:**

1) **Improved bone regeneration using bone anabolic drug conjugates (C3 and C6) with deproteinized bovine bone mineral as a carrier in rat mandibular defects**

Objective: Deproteinized bovine bone mineral (DBBM) has been extensively studied and used for bone regeneration in oral and maxillofacial surgery. However, it lacks an osteoinductive ability. We developed two novel bone anabolic conjugated drugs, known as C3 and C6, of an inactive bisphosphonate and a bone activating synthetic prostaglandin agonist. The aim was to investigate whether these drugs prebound to DBBM granules have the potential to achieve rapid and enhanced bone regeneration.

Methods: Bilateral defects (4.3 mm diameter circular through and through) were created in mandibular angles of 24 Sprague-Dawley rats were filled with DBBM Control, DBBM with C3 or DBBM with C6 (n = 8 defects per group/ each timepoint). After 2 and 4 weeks, postmortem samples were analyzed by microcomputed tomography followed by backscattering electron microscopy and histology.

Results: DBBM grafts containing the C3 and C6 conjugated drugs showed significantly more bone formation than DBBM control at 2 and 4 weeks. The C6 containing DBBM demonstrated the highest percentage of new bone formation at 4 weeks. There was no significant difference in the percentage of the remaining graft between the different groups at 2 or 4 weeks.

Conclusions: DBBM granules containing conjugated drugs C3 and C6 induced greater new bone volume generated and increased the bone formation rate more than the DBBM controls. This is expected to allow the development of clinical treatments that provide more predictable and improved bone regeneration for bone defect repair in oral and maxillofacial surgery.

2) **Achieving enhanced bone regeneration using monetite granules with bone anabolic drug conjugates (C3 and C6) in rat mandibular defects**

Bone grafting procedures are commonly used to manage bone defects in the craniofacial region. Monetite is an excellent biomaterial option for bone grafting, however, it is limited by lack of osteoinduction. Several molecules can be incorporated within the monetite matrix to promote bone regeneration. The aim was to investigate whether incorporating bone forming drug conjugates (C3 and C6) within monetite can improve their ability to regenerate bone in bone defects. Bilateral bone defects were created in the mandible of 24 Sprague–Dawley rats and were then packed with monetite control, monetite+C3 or monetite+C6. After 2 and 4 weeks, post-mortem samples were analyzed using microcomputed tomography, histology and backscattered electron microscopy to calculate the percentages of bone formation and remaining graft material. At 2 and 4 weeks, monetite with C3 and C6 demonstrated higher bone formation than monetite control, while monetite+C6 had the highest bone formation percentage at 4 weeks. There were no significant differences in the remaining graft material between the groups at 2 or 4 weeks. Incorporating these anabolic drug conjugates within the degradable matrix of monetite present a promising bone graft alternative for bone regeneration and repair in orthopedic as well as
oral and maxillofacial applications.

Response to the following questions:

1. Were the original, specific aims of the proposal realized? Yes

2. Were the results published? Yes
   a. If so, cite reference/s for publication/s including titles, dates, author or co-authors, journal, issue and page numbers.

   1) **Sheikh Z*, Abdallah MN***, Al-Jaf F, Chen G, Hamdan N, Young RN, et al. Achieving enhanced bone regeneration using monetite granules with bone anabolic drug conjugates (C3 and C6) in rat mandibular defects. J Biomed Mater Res B Appl Biomater. 2020 Mar 11 (***Equal contribution**).

   2) **Sheikh Z***, **Abdallah MN***, Al-Jaf F, Chen G, Hamdan N, Young RN, Grynpas MD, Glogauer M. *Improved bone regeneration using bone anabolic drug conjugates (C3 and C6) with deproteinized bovine bone mineral as a carrier in rat mandibular defects*. J Periodontol. 2020 [Ahead of print] (***Equal contribution**).

   b. Was AAOF support acknowledged? Yes

3. Have the results of this proposal been presented? Yes

   a. If so, list titles, author or co-authors of these presentation/s, year and locations

   1) Oral presentation: **Abdallah MN**, Sheik Z, Al-Jaf F, Chen G, Young R, Hamdan N, Glogauer M, Grynpas M. *Use of a novel anabolic conjugate drug on a synthetic biomaterial for enhancing bone regeneration in critical-sized bone defects*. Latest advances in Canadian Orthodontic Research, Canadian Association of Orthodontists, 71st Annual Scientific session. Fredericton-NB, Canada. September 2019.

   2) Oral presentation (cancelled due to the COVID-19 pandemic): **Abdallah MN**, Sheik Z, Al-Jaf F, Chen G, Young R, Hamdan N, Glogauer M, Grynpas M. *anabolic bone drug complexes with a bioresorbable synthetic biomaterial for enhanced bone regeneration*. American Association of Orthodontists, Oral Research Presentation, Washington, USA. May 2020.

   b. Was AAOF support acknowledged? Yes

4. To what extent have you used, or how do you intend to use, AAOF funding to further your career?

The AAOF RAA is an incredible resource for orthodontic residents to help with conducting their research. The funding and support of this award was essential for the completion of this project and was used to cover part of the budget required for characterizing the animal specimens. Furthermore, obtaining the AAOF funding has reinforced my career goal in becoming a clinician-scientist in academia.