***Please note: Dr. Frazier-Bowers submitted a combined revised Final Report for both her 2001 and 2002 Orthodontic Faculty Development Fellowship Awards and thus these are duplicates of each other.***

# AAO Foundation Award Final Report

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| Principal Investigator | Sylvia A. Frazier-Bowers |
| Co-Investigator | |
| Secondary Investigators | |
| Award Type | Faculty Development Award |
| Project Title | The Genetic Basis of Tooth Agenesis |
| Project Year | 2002 – continuation from 2001 |
| Institution | The Univ. of Texas Health Science Center and Univ of North Carolina at Chapel Hill |
| Summary/Abstract (250 word maximum) | The AAOF Faculty Development Award served as an impetus for my career goal, which is to combine clinical practice and research in an academic setting. As a result of the AAOF award my research led to the identification of novel mutations, single nucleotide polymorphisms (SNPs) responsible for congenital missing teeth in two genes, *PAX9* and *MSX*. Experiments that led to these findings included genotyping, linkage analysis, mutational analysis of *PAX9* and *MSX1* performed on DNA samples from families affected with hypodontia. Progress also includes genotyping and mutational analysis of Vietnamese individuals affected with a unique form of tooth agenesis. While we have not yet identified the causative mutation, we are working on data that suggests a novel gene responsible for this pattern of human tooth agenesis. The most promising outcome of this funding is that it resulted in the funding of an NIH K23 award to continue studies that decipher the complex genetic contribution to a common tooth disorder. Finally, my development in research occurred concurrently with continuing education and activities in clinical orthodontics. I have maintained clinical practice activities while participating on committees of organized dentistry both locally and nationally. As part of this Faculty Development Award, my teaching portfolio was expanded, which initiated with single lectures but resulted in serving as course director for multiple courses. In summary, the AAOF has afforded me the opportunity to develop significantly in the research tract and considerably in teaching and clinical endeavors. |
| Were the original, | Since this was a Faculty Development Awards, the specific aims of this project including specific research studies on the genetic of |

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| specific aims of the proposal realized? | missing teeth and later eruption failure, but also teaching and career development plans. Research specific aims include: **Aim 1: To identify, clinically characterize, and collect samples from families with several members demonstrating multiple patterns of congenitally missing teeth, and from individuals with this condition who do not have a family history**.<br><br>**Aim 2: To identify *MSX1* and *PAX9* mutations associated with molar oligodontia by sequencing these genes in 28 existing and new individuals affected with molar oligodontia identified from aim 1**.<br><br>**Aim 3**: **To determine the chromosomal location of the gene causing non-syndromic mandibular incisor agenesis using DNA from families identified in aim 1**. |
| Were the results published? If not, are there plans to publish? If not, why not? | There were several publications stemming from these studies (*some with collaborators*). They are as follows:<br><br>1. ***Frazier-Bowers, S. A***., Pham, K.Y., Le, E. V., Cavender, A.C., Kapadia, H., King, T.M., Milewicz, D.M., D'Souza, R.N. A Unique Form of Hypodontia Observed in Vietnamese Patients: Clinical and Molecular Analysis. ***J Med Genet.*** **2003 Jun;40(6):e79**<br><br>2. ***Frazier-Bowers, S***., Scott, M.R., J, Mensah, D'Souza, R.N. Mutational Analysis of Families Affected with Molar Oligodontia. ***Connective Tissue Research,*** **43: 1-5, 2002**<br><br>3. ***Frazier-Bowers, S.A*****. Guo, D.C., Cavender, A., King, T., Xue, L., Evans, B., Milewicz, D., D'Souza. A Novel Mutation in Exon 4 of Human *PAX9* Causes Molar Oligodontia.** ***Journal of Dental Research,*** **81 (2): 129-133, 2002**<br><br>4. Kapadia, H, ***Frazier-Bowers, S. A***., Ogawa, T, and D'Souza, R. Molecular characterization of a novel *PAX9* missense mutation causing posterior tooth agenesis. ***European Journal of Human Genetics***. **2006** Apr;14(4):403-409**.**<br><br>5. ***Frazier-Bowers, SA,*** Koehler, K, Ackerman, J, Proffit, W. Primary Failure of Eruption: Further Characterization of a Rare Eruption Disorder, ***J Orthodontics and Dentofacial Orthopedics*** **2007 *May*;131(5):578.e1-11**.<br><br>6. ***Frazier-Bowers, S***., Scott, M.R., J, Mensah, D'Souza, R.N. Mutational Analysis of Families Affected with Molar Oligodontia. ***Connective Tissue Research,*** **43: 1-5, 2002** |
| Have the results of this | ***Here are abstracts from AADR/IADR and other meetings related to*** |

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| proposal been presented? If so, when and where? If not, are there plans to do so? If not, why not? | ***this project:***<br><br>1. Corbin, CM, Scruggs, W, Burns, E, and ***Frazier-Bowers, S.A***. Evaluating Non-coding Regions of *PAX9* in Patients with Tooth Agenesis. ***J. Dent. Res.* 81 SI-A 2006**.<br><br>2. Ogawa* T., Berrocal, M.C., Kapadia, H.,Olfert, K., **Frazier-Bowers, S.A**. and D'Souza, R.N. The potential genetic modifiers of the Pax9-Msx1 pathway ***J Dent Res 84(Spec Iss A):(0028), 2005***<br><br>3. **Frazier-Bowers*, S.A**., Cavender, Berrocal, M.C, Cavender, A.C, King, T, Guo, D, Milewicz, D, and D'Souza, R.N. Examining the Role of Candidate Genes in X-linked Tooth Agenesis ***J. Dent. Res, Vol. 82 SI A 2004***<br><br>4. **Frazier-Bowers*, S.A**., Berrocal, M.C, and D'Souza, RN. Identification of a *MSX1* Polymorphism in Families with *PAX9* Mutations. ***J. Dent. Res, Vol. 82 SI A 2004***<br><br>5. E.V. LE, Berrocal, M.C, D'Souza, R.N and **Frazier-Bowers, S.A** Mutational Analysis of dHAND and IKKa in Mandibular Incisor Agenesis ***J. Dent. Res, Vol. 82 SI A 2004***<br><br>6. **Frazier-Bowers*, S.A**., Cavender, A.C., Guo, D. Milewicz, D. and D'Souza, R. A Novel Mutation in *MSX1* is Associated with Selective Posterior Tooth Agenesis. ***J. Dent. Res, Vol. 82 SI A 2003***<br><br>7. Clinical and Molecular Analysis of Mandibular Incisor Agenesis in Vietnamese Patients. Le, E, Pham, K., King, T., D'Souza, R.N., **Frazier-Bowers, S.A**. ****student winner of Hinman, October, 2002.***<br><br>8. E.V.Le*, Pham, K., King, T., Milewicz, D., Cavender, A., King, D'Souza, R.N, **Frazier-Bowers, S.A**. A Unique Form of Hypodontia Observed in Vietnamese Patients: Clinical and Molecular Analysis. ***J. Dent. Res, Vol. 82 SI A 2003***.<br><br>9. Hanis*, S.B., Milewicz, D.,D'Souza, R.N., **Frazier-Bowers, S.A**. Determining the Genetic Basis of Non-Familial Tooth Agenesis. ***J. Dent. Res, Vol. 82 SI A 2003***<br><br>10. *PAX9* and *MSX1* as partners in Tooth Development. Mensah*, J.K., Wang, B., Kapadia, H. Cavender, A., **Frazier-Bowers, S.A.**, D'Souza, R.N. ***J. Dent. Res, Vol. 82 SI B 2003*** |

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| | 11. **Frazier-Bowers*, S.A**. Guo, D.C., Cavender, A., King, T., Xue, L., Evans, B., Milewicz, D., D'Souza. A Novel Mutation in Exon 4 of human *PAX9* Causes Molar Oligodontia. ***J. Dent. Res.* 81 SI- A, 2002**.<br><br>12. Jackson*, A., Frazier-Bowers, S., and D'Souza, R. A Novel Mutation in the Paired Domain of PAX9 Causes Molar Oligodontia. ***J. Dent. Res.* 81 SI- A, 2002**. ***winner of Craniofacial Biology Sarnat Award***<br><br>13. Frazier-Bowers*, S, Scott, M.R., Cavender, A., Mensah, J., and D'Souza, R.N. Mutational Analysis of Families Affected with Molar Oligodontia. ***Connective Tissue Research* 2002** |