Oral Microbiome and Systemic Health

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Genomic Medicine IV

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NHGRI (Ian Marpuri)
Oral Microbiome and Systemic Health Research Project

**Goal:** to establish an Oral/Systemic Health Cohort for research across multiple institutions

**Process:** standardized enrollment of patients with EHR and EDR, standardized clinical tests, standardized microbiome characterization, genomic DNA, plasma and serum to advance Translational Medicine and Dental Care
Marshfield Clinic
Mount Sinai School of Medicine
Morehouse School of Medicine
University of Pittsburgh
University of Pennsylvania
Ohio State University Medical Center
University of North Carolina
University of Medicine and Dentistry of New Jersey
University of Illinois at Chicago
Cleveland Clinic
Case Western Reserve University
Spoiler Alert

• The mouth is part of the body

• The microbiome needs to be factored in for risk assessment for some of the most common and costly diseases

• Microbiome must be part of Personalized Medicine

• A consortium of patient cohorts with standardized recruitment, sample collection and data will advance the field
GENETICS ← ENVIRONMENT

Diet ← Microbiome

COMPLEX DISEASE

T2D, RA, CAD
Enhance prediction
health disparities
Oral Systemic Health Research Project

Progress to date:

• Series of conference calls to plan the initiative
• Organizing National Oral Systemic Health Consortium with standardized recruitment criteria
• Phase I (Pilot Project) completed at Marshfield
• Standardized recruitment
• Standardized sample collection
• Standardized questionnaire
• 41 patients enrolled – added to PMRP cohort
• Published manuscript outlining the project
• Planned enrollment of (Phase II) 2,000 additional subjects at Marshfield Clinic
• Planned enrollment of 400 subjects at Mt. Sinai
Oral Systemic Health Research Project

- Long term EMR Data
- Host DNA Data
- Oral Microbiome Data
- EDR Data
- Plasma & Serum Samples
- Standard Clinical Tests at enrollment
• Inclusion/Exclusion criteria
• Periodontitis case definition
• Types of oral samples to be collected
• Number of oral samples to be collected per patient
• Timing of collection of samples
• Ability to follow-up patient after initial sample collection
• Method for collection of oral samples
• Method for extraction of nucleic acids from oral microbiome samples
• Method for identifying microbial species present in the oral samples
• Methods for other ‘omics
• Other types of biological samples to be collected
• Other primary phenotypes of interest
The oral-systemic personalized medicine model at Marshfield Clinic

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Periodontal disease and diabetes, two diseases that have achieved epidemic status, share a bidirectional relationship driven by micro-inflammatory processes. The present review frames the current understanding of the pathological processes that appear to link these diseases and advances the hypothesis that reversal of the epidemic is possible through application of interdisciplinary intervention and advancement of oral-systemic personalized medicine. An overview of how Marshfield Clinic’s unique clinical, informatics and bio-repository resources and infrastructures are being aligned to advance oral-systemic personalized medicine is presented as an interventional model with the potential to reverse the epidemic trends seen for these two chronic diseases over the past several decades. The overall vision is to engineer a transformational shift in paradigm from ‘personalized medicine’ to ‘personalized health’.

However, existing attempts at epidemiological prevalence projections support Satcher’s characterization, with estimates of 75% of the US population affected by gingivitis, 35% of adults affected by periodontal disease (PD), and approximately 13% afflicted by severe periodontitis, with persons of low socioeconomic status disproportionately affected (Albandar et al., 1999). Emerging evidence that PD impacts exacerbation of other pathological conditions systemically has heightened concern over the high prevalence of oral disease. Of highest concern was mounting evidence demonstrating that diabetes mellitus (DM), another escalating epidemic, and PD represented reciprocal risk and exacerbation factors for each other, presumably mediated by chronic inflammatory pathophysiological mechanisms (Mealey et al., 2006). However, a critically important finding of some studies was that, with appropriate oral prophylaxis and intervention, exacerbation of both conditions could
<table>
<thead>
<tr>
<th>2012*</th>
<th></th>
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<tbody>
<tr>
<td>No. Dental Centers</td>
<td>9</td>
</tr>
<tr>
<td>Square Feet</td>
<td>114,181</td>
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<tr>
<td>Total Operatories</td>
<td>182</td>
</tr>
<tr>
<td>Training Operatories</td>
<td>24</td>
</tr>
<tr>
<td>Dental Students</td>
<td>0</td>
</tr>
<tr>
<td>Dentists (includes general dentists, oral surgeons, and a pediatric dentist)</td>
<td>52</td>
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<tr>
<td>Total FTEs</td>
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*includes Black River Falls clinic, opening this year
### Pilot: Clinical Results to Date

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<tr>
<th>Cut off value for notification</th>
<th>No. subjects at visit 1 n=41</th>
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<tr>
<td>Cholesterol &gt;200</td>
<td>16</td>
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<tr>
<td>Fasting blood glucose &gt;100</td>
<td>14</td>
</tr>
<tr>
<td>Microalbumin &gt;1</td>
<td>11</td>
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<tr>
<td>ave left systolic BP &gt;140</td>
<td>4</td>
</tr>
<tr>
<td>ave right systolic BP &gt;140</td>
<td>4</td>
</tr>
<tr>
<td>ave left diastolic BP &gt;90</td>
<td>2</td>
</tr>
<tr>
<td>ave right diastolic BP &gt;90</td>
<td>4</td>
</tr>
<tr>
<td>hs-CRP &gt;3</td>
<td>16</td>
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<tr>
<td>HbA1c &gt;7</td>
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<tr>
<td>TOTAL</td>
<td>71</td>
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<table>
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<th>No. lab values per person triggering notification</th>
<th>No. subjects at visit 1 n=41</th>
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<tr>
<td>1 value</td>
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<tr>
<td>2 values</td>
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<tr>
<td>3 values</td>
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<tr>
<td>4 values</td>
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<tr>
<td>5 values</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>35</td>
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Age and T2 Diabetes Distribution of OSRP Pilot Subjects at Enrollment (n=41)

- Orange bars represent T2DM diagnosis
- Blue bars represent No T2DM Diagnosis

No. Subjects

Age in years

- 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74

Marshfield Clinic

15... Don't just live. Shine.
Fasting Glucose and T2 Diabetes Distribution of OSRP Pilot Subjects at Enrollment (n=41)

T2DM diagnosis  No T2DM diagnosis

No. Subjects

Fasting Glucose (mg/dL)

65 68 71 74 77 80 83 86 89 92 95 98 101 104 107 110 113 116 119 122 125 128 131 134 137 140 143 146 149 152 155
C reactive Protein results

High Sensitivity C-Reactive Protein Distribution of OSRP Pilot Subjects at Enrollment (n=41)

<table>
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<tr>
<th>hs-CRP [mg/L]</th>
<th>cardiovascular risk</th>
<th>no. subjects</th>
<th>% subjects</th>
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<tr>
<td>&lt;1</td>
<td>low risk</td>
<td>10</td>
<td>24.39</td>
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<tr>
<td>1-3</td>
<td>average risk</td>
<td>15</td>
<td>36.59</td>
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<tr>
<td>&gt;3</td>
<td>high risk</td>
<td>16</td>
<td>39.02</td>
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We will continue efforts to form a network of like-minded institutions across the country to establish a large and diverse cohort of dental/medical patients with EHRs, EDRs and oral microbiome samples.

In addition to T2D, RA and CAD, this cohort can be used to implement PGx in dentistry, including pain control and coagulation management.
Acknowledgements

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- MFLD Clinic laboratory staff

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