Avellino Labs

THE FUTURE OF PRECISION MEDICINE

Eric Bernabei
Chief Sales and Marketing Officer
Avellino Labs

Genetic services provider specializing in data, diagnostics, and therapies.

- **‘08**: 1st PCR genetic test to detect corneal dystrophy
- **‘15**: Named Technology Pioneer - World Economic Forum
- **‘16**: Partnered with Ulster University to develop novel gene editing treatments
- **‘19**: Launch AvaGen NGS test for KC Risk Factors / TGFBI CD
Avellino Labs

Pioneering Precision Medicine for Eye Care and Beyond
Proven Scientific Leadership & Clinical Advisors

John Marshall, PhD, MBE
Board Member
Director of Scientific and Medical Affairs

Tara Moore, PhD
Professor of Personalized Medicine, Ulster Univ, Chief R&D Officer

Edward Holland, MD
Eric Donnenfeld, MD
Terry Kim, MD
Dick Lindstrom, MD

David Hwang, MD
Andrea Cusumano, MD
Elizabeth Yeu, MD
Vance Thompson, MD

Burkhard Dick, MD
EK Kim, MD, PhD
Shigeru Kinoshita, MD
Aaron Lech, OD
Introducing AvaGen

After 10 years of development, the first and only NGS test combining CD Testing and KC Risk Scores

- 2008: Test for 1 TGFBI mutation (GCD2)
- 2014: Test for 2 TGFBI mutations (GCD1, GCD2)
- 2015: Universal 5 GCD1, GCD2, LCD1, TBCD, RBCD
- 2017: R&D Identified 6 more TGFBI mutations LCD I/IIA, 2 vt LCD, variant TBCD, GCD, RBCD

70 CD TGFBI mutations +
Over 1,000 variants across 75 genes associated with KC
Join Us Sunday Evening!

PREMIERE SCREENING

PLEASE JOIN US FOR AN ADVANCED SCREENING OF OUR ADVANCED SCREENING

Avellino Labs, a global leader and pioneer in precision medicine, will proudly unveil our next generation sequencing (NGS) genetic technology for the diagnosis of keratoconus and TGFBI corneal dystrophies.

This momentous event will include presentations by:

- Eric D. Donnenfeld, MD
- Edward J. Holland, MD
- Terry Kim, MD
- Richard L. Lindstrom, MD
- Elizabeth Yeu, MD

WHERE
Blue Shield of California Theater at YBCA
700 Howard Street
San Francisco, CA 94103
(across the street from the Moscone Center)

WHEN
Sunday, October 13, 2019
5:30-6:30PM
Cocktails and Appetizers
6:30PM-7:30PM
Enjoy the show!
Why a Genetic Test for Keratoconus?

Don’t we already know the etiology?

There is no one gene responsible for the development of keratoconus but there is a strong genetic component or link within each group.¹

Understanding the Natural Progression of Keratoconus

Systematic review and meta-analysis of 11,529 eyes with untreated keratoconus to identify predictors of progression

Middle Eastern populations

• experienced significantly greater $K_{\text{max}}$ increase than Europeans and East Asians

1.23 D (95% CI: –0.33 to 2.80) vs 0.75 D (95% CI: –0.15 to 1.66; $P=0.01$) and 0.16 D (95% CI: –0.34 to 0.66; $P=0.01$), respectively

Younger patients

• Patients were predicted to have 0.8 D less $K_{\text{max}}$ steepening over 12 months for every 10-year increase in age

• Patients <17 years old are likely to have more than 1.5 D of $K_{\text{max}}$ progression over 12 months

Patients with greater $K_{\text{max}}$ at baseline

• Patients were predicted to have a 1 D greater $K_{\text{max}}$ steepening for every 5 D greater baseline $K_{\text{max}}$

• Patients with >55 D $K_{\text{max}}$ at baseline are likely to progress by at least 1.5 D $K_{\text{max}}$ at 12 months

Global Keratoconus Risk

Millions of patients are at risk based on corneal curvature alone

309,000,000
Patients with >46D corneal curvature or >2D cylinder

90%
Live in Asia-Pacific Countries
60% in India and China

1,700,000
Between ages 15-30 yrs old,

4,000
Cornea Specialists
Keratoconus Risk in US & Canada

Population ≤ 46D Central K 364.9M

- K ≤ 46D & ≥ 2D Cyl: 8.4 million people
- K ≤ 46D & ≥ 2D Cyl Age 15-30: 0.1 million people
- K ≤ 46D & ≥ 2D Cyl Age 15-30 & Access to Care: 0.1 million people

Population ≥ 47D Central K 3.1M

- ≥ 47D to < 48D At Risk: 2.6 million people
- ≥ 48D Keratoconus: 0.5 million people
- ≥ 48D & Access to Care: 0.4 million people

Slide courtesy of MarketScope.
Identifying At Risk Patients

Patients with higher than normal risk for triggering or natural progression of disease

- Patients with >47D cc and/or >2D astigmatism
- Contact Lens and Orthokeratology Candidates
- Refractive Surgery Candidates
- Family History of Keratoconus
Using Genetic Testing to Identify Patients at Risk

Testing Process:

Extraction → Sequencing → Referencing and Variant Risk Scores → Patient Report
**Reading Results**

**Individual variants receive risk scoring for KC, description for TGFBI CD**

- **98% Accuracy** in detecting targeted genes and variants – Proven in CLIA validation, September 2019
- All variants carry a risk. If it’s on the report, some level of risk is identified.
- Negative result = no risk variants found.
- Genetic counselors perform interpretation and will be made available for physicians and patients

<table>
<thead>
<tr>
<th>Gene</th>
<th>Transcript</th>
<th>cDNA</th>
<th>Zygosity</th>
<th>AA Change</th>
<th>RiskScore†</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>NM_000093.4</td>
<td>c.C4135T</td>
<td>Homozygous</td>
<td>p.P1379S</td>
<td>68.45</td>
<td>High Risk</td>
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<tr>
<td>NM_000428.2</td>
<td>c.G2344C</td>
<td>Homozygous</td>
<td>p.E782Q</td>
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<td>NM_000428.2</td>
<td>c.G2326A</td>
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<td>p.V776I</td>
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<td>Low Risk</td>
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<tr>
<td>NM_001127464.1</td>
<td>c.C8260T</td>
<td>Homozygous</td>
<td>p.H2754Y</td>
<td>37.36</td>
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<tr>
<td>NM_001127464.1</td>
<td>c.G8272A</td>
<td>Homozygous</td>
<td>p.E2758K</td>
<td>40.38</td>
<td>Medium Risk</td>
<td></td>
</tr>
</tbody>
</table>

**Risk Score Reference Bar:**

- 0 = Very Low
- 20 = Low
- 40 = Medium
- 60 = High
- 80 = Very High

<table>
<thead>
<tr>
<th>Gene</th>
<th>Transcript</th>
<th>cDNA</th>
<th>Zygosity</th>
<th>AA Change</th>
<th>Reported phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGFBI</td>
<td>NM_000358.2</td>
<td>c.1631A&gt;G</td>
<td>Homozygous</td>
<td>p.N544S</td>
<td>Corneal dystrophy, lattice intermediate type I/III A</td>
</tr>
</tbody>
</table>
Positive Disruption: Next Gen Testing, Big Data, and AI

AI Driven Molecular Network Mapping and Pairwise Risk Scores
AvaGen™ Capability Pipeline

Continuous addition of detection capabilities will make AvaGen THE genetic eye test.

**Front**

- **2008 - 2019**: Corneal Dystrophies, Keratoconus
- **2019 - 2020**: Fuchs ECD, EBMD, Fleck CD, Macular CD, Schnyder CD

**Middle**

- **2021+**: Glaucoma, Cataract, Myopia, Presbyopia, Hyperopia
- **Uveitis**

**Back**

- **2020+**: Retinitis Pigmentosa, AMD, Stargardt’s Disease
• Early detection of risk factors and diseases
• Education about monitoring and treatment options
• Empowering physicians and patients