# Dynamis Therapeutics, Inc.

## Fox Chase Cancer Center
## Research and Technology Symposium
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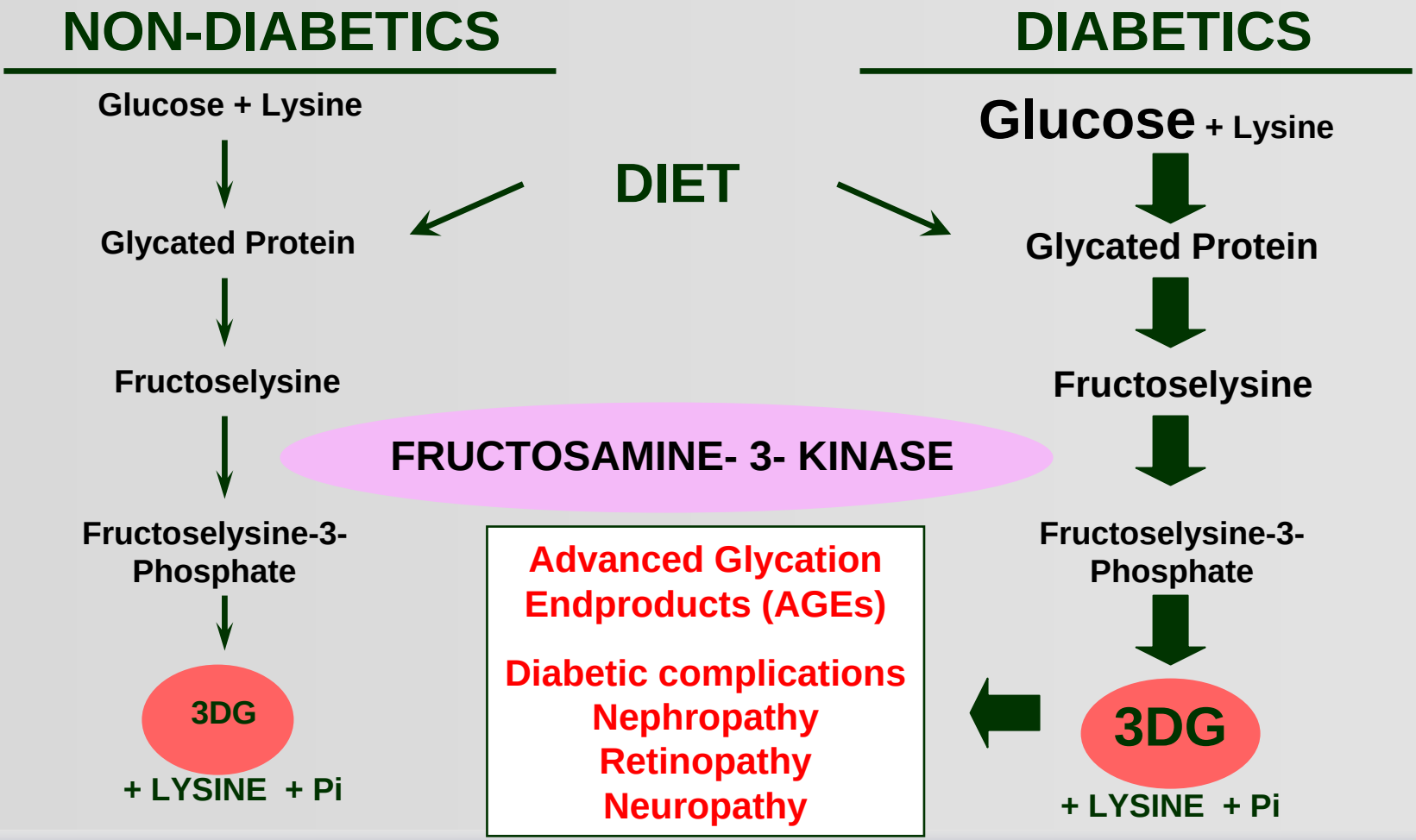
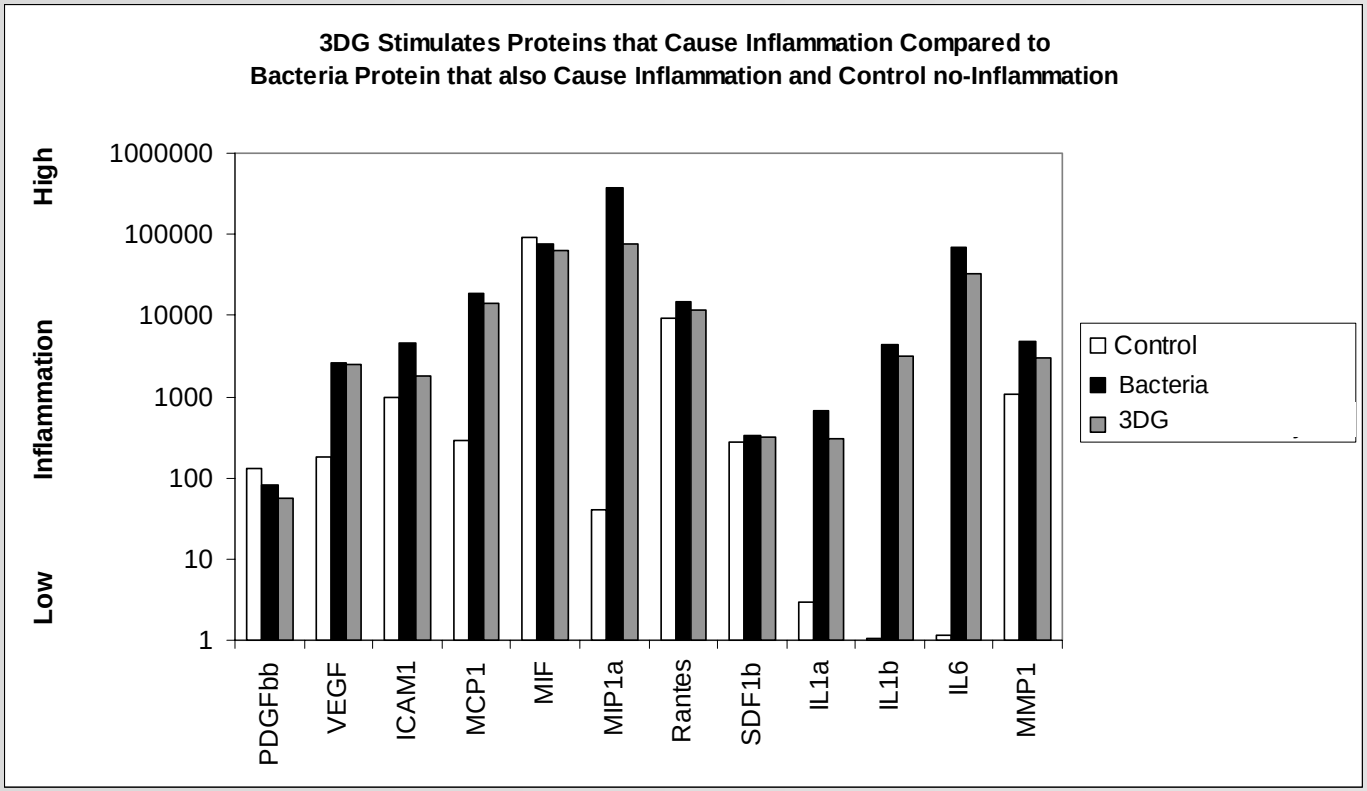
# *Dynamis Therapeutics, Inc.*

- A private, pharmaceutical company, spun out from the Fox Chase Cancer Center (FCCC), became operational in 2002
- 9 full time employees, plus consultants, labs at FCCC and the PA College of Optometry, offices in Jenkintown, PA
- $9.4 million in investment and grants
- Extensive worldwide patent portfolio
- Cosmetic total sales and licensing fees of $2.1 million.

# Fructosamine –3-Kinase Pathway

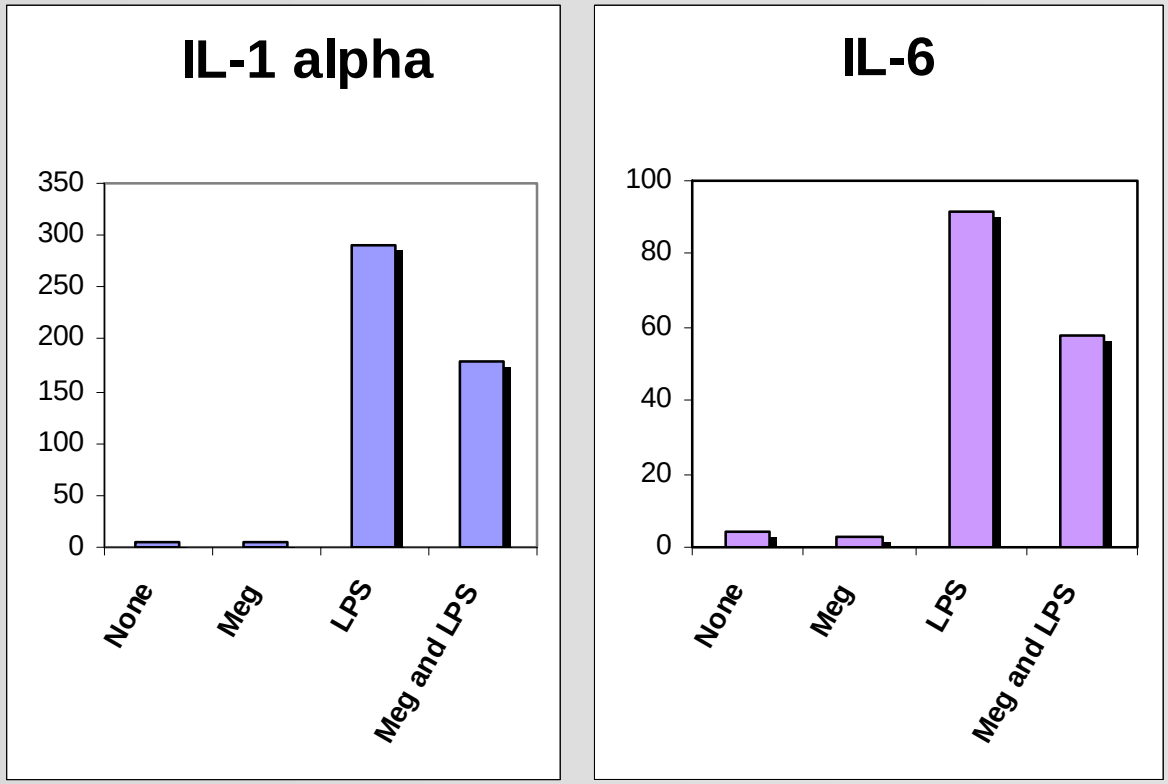


# Laboratory studies confirm 3DG causes inflammation




**Peripheral blood mononuclear cells treated with LPS or fructoselysine (precursor of 3DG). Immunomodulators released were measured by ELISA.**

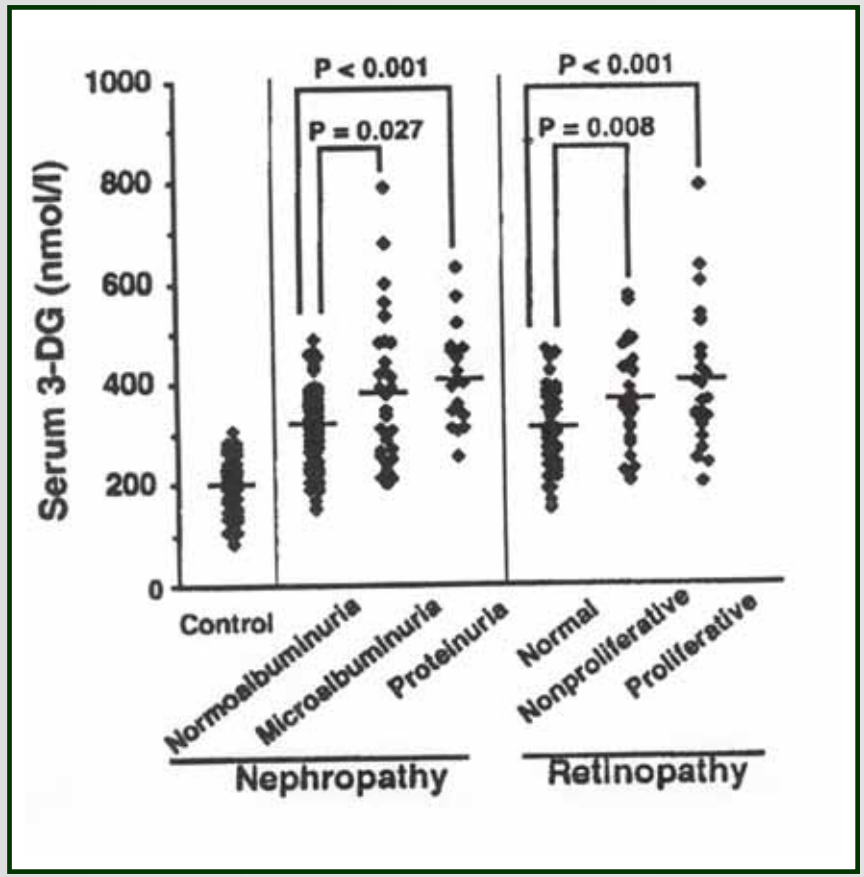
# Laboratory Studies Confirm Meglumine Inhibits Inflammation




**U937 Promonocytic Cells stimulated with LPS and treated with 50mM Meglumine. Cytokine release measured by ELISA.**

# Elevated 3DG Levels Linked to Diabetic Kidney and Eye Disease

- Cohort of 110 diabetics and 57 control subjects examined
- Increases in serum 3DG levels correlate with extent of nephropathy and retinopathy

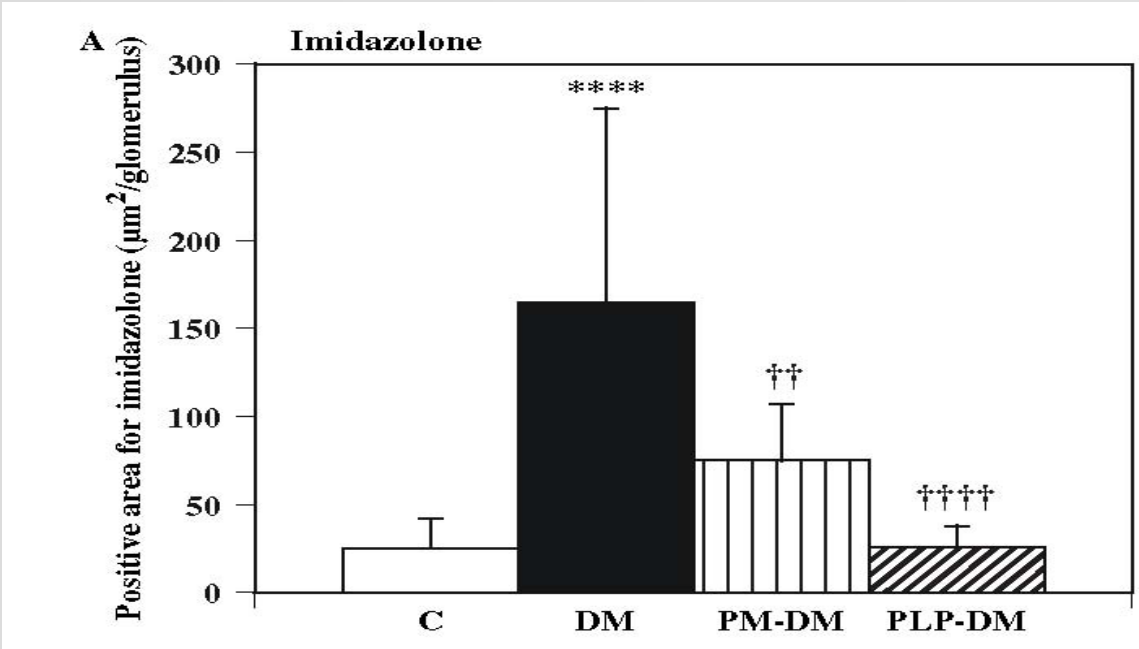



*Kusunoki et al., Diabetes Care 26:1889 (2003)*

# 3DG Inactivator Leads to Improved Diabetic Kidney Function

## Treatment of diabetic rats with pyridoxal-phosphate (PLP) for 16 weeks:

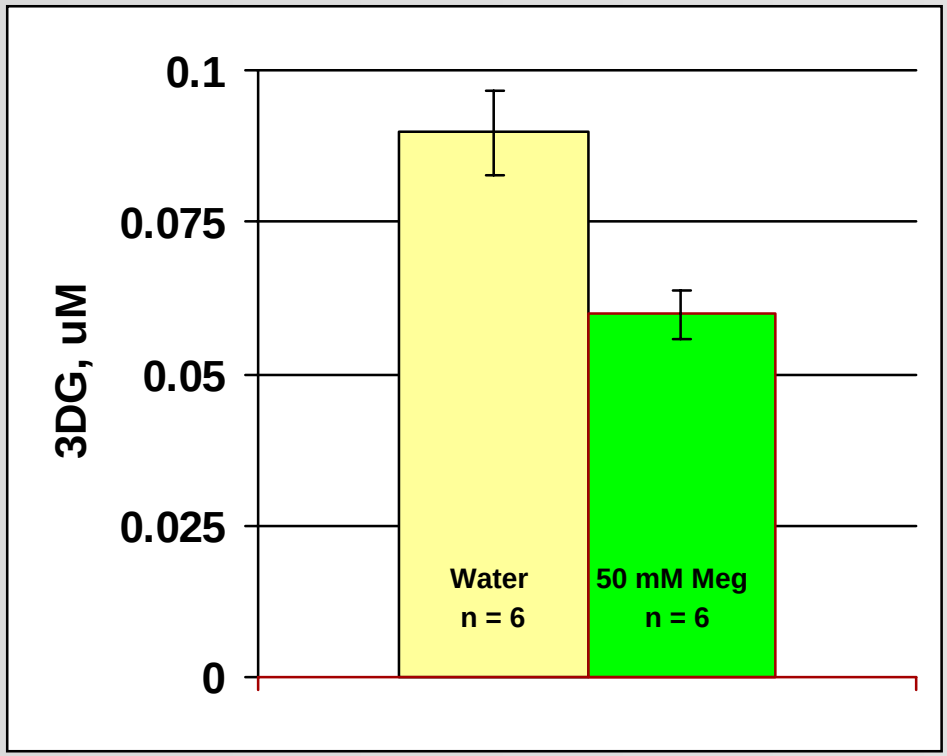
- Lowers 3DG derived AGEs in kidney (shown)
- Prevents progression of nephropathy
- Lowers RAGE




*Nakamura et al., (2007) Nephrol. Dial. Transplant 22:2165-74*

# Dynamis' Compound Controls 3DG in Rats Orally Dosed for 32 weeks- Urinary 3DG

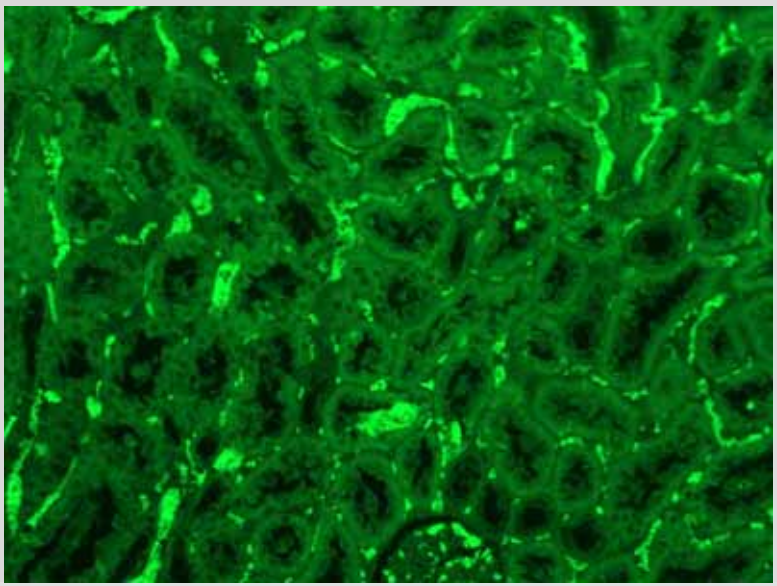
**Rats treated with meglumine in their drinking water for 32 weeks have lower levels of 3DG (p=0.005).**



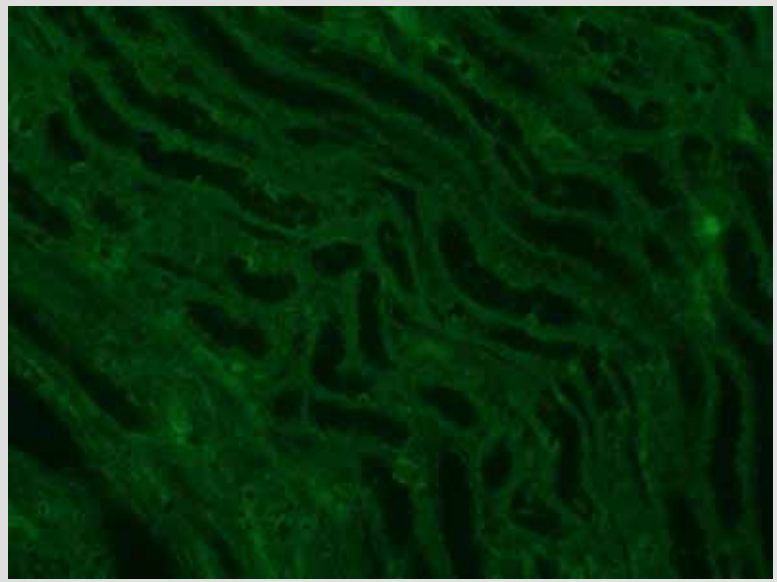
# *Dynamis' Compound Controls AGE Production in Rats Orally Dosed For 32 Weeks—Kidney Tubules*

**Bright green (fluorescent antibody to imidazolone AGE) indicates the presence of AGE in the non-treated control rats vs absence of bright green in rats treated with AGE inhibitor indicating no AGE is present in aging rat.**

**Imidazolone Antibody Control**



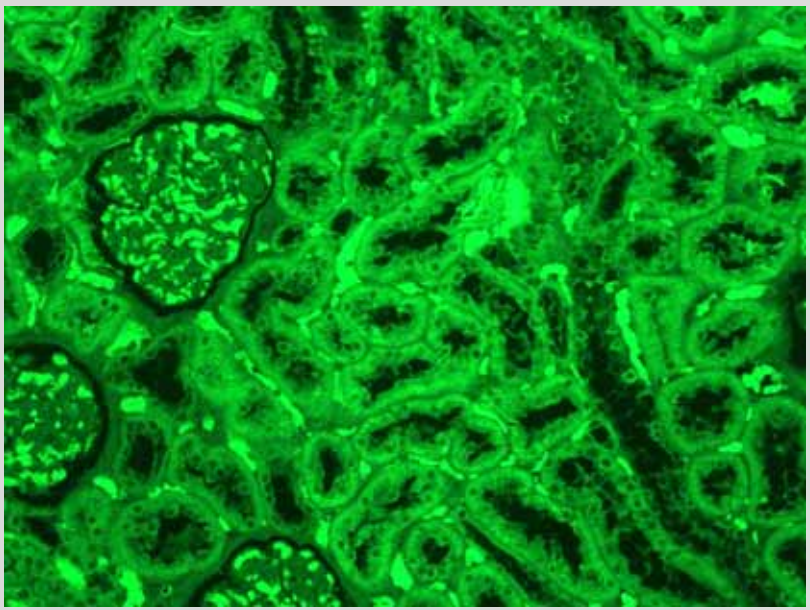
**Imidazolone Antibody Meglumine Treated**



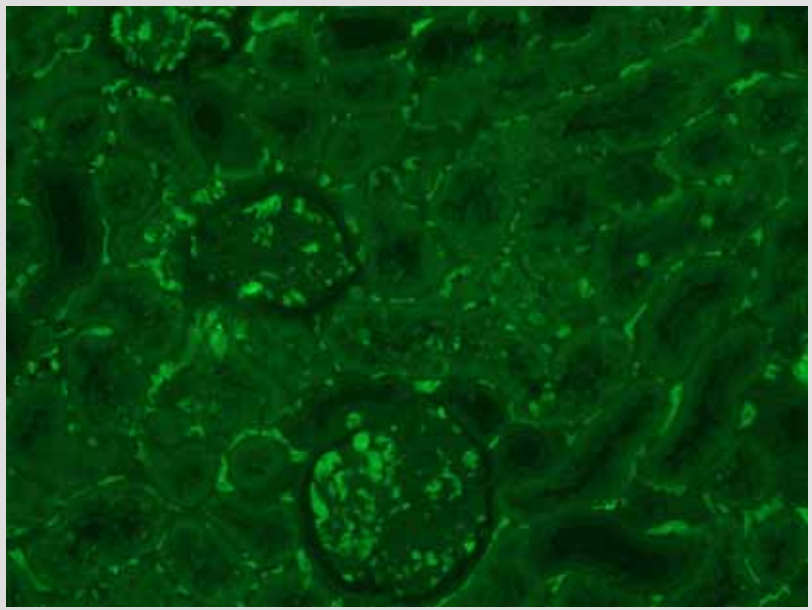
# *Dynamis' Compound Controls AGE Production in Rats Orally Dosed For 32 Weeks—Kidney Glomeruli*

**Bright green (fluorescent antibody to imidazolone AGE) indicates the presence of AGE in the non-treated control rats vs absence of bright green in rats treated with AGE inhibitor indicating no AGE is present in aging rat**

**anti-Imidazolone Antibody Control**



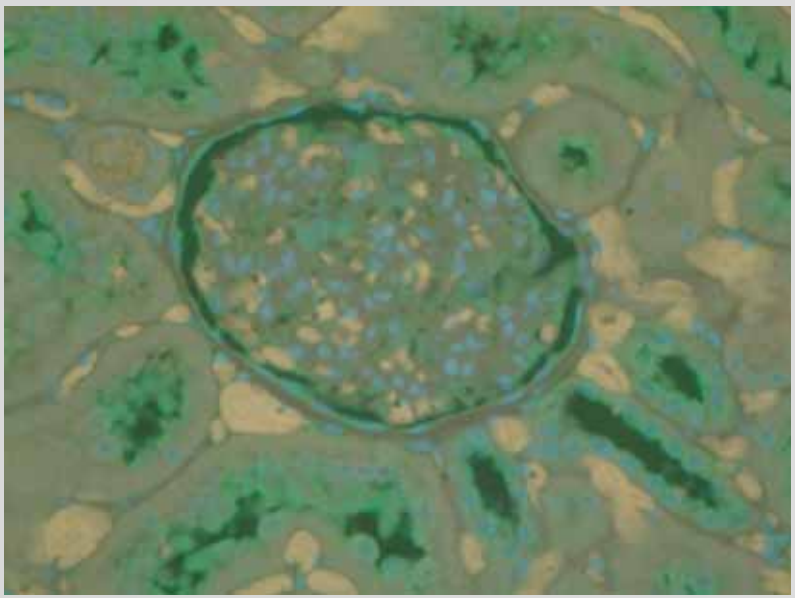
**anti-Imidazolone Antibody Meglumine Treated**



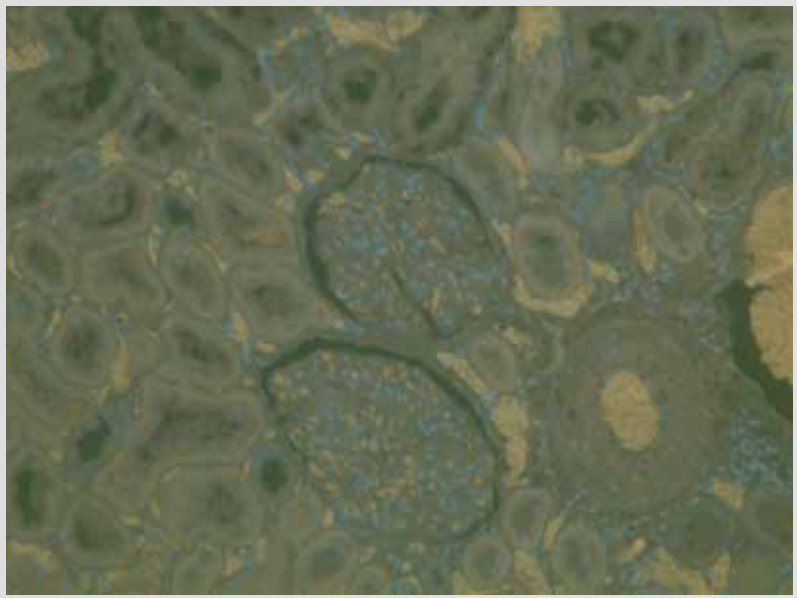
# Dynamis' Compound Controls RAGE Production in Rats Orally Dosed for 32 Weeks—Kidney Glomerulus

**Bright green (Florescent antibody to RAGE) indicates the presence of RAGE in the non-treated control rats vs absence of bright green in rats treated with RAGE inhibitor indicates no RAGE has formed with aging**

**RAGE Antibody**
**Control Rat**



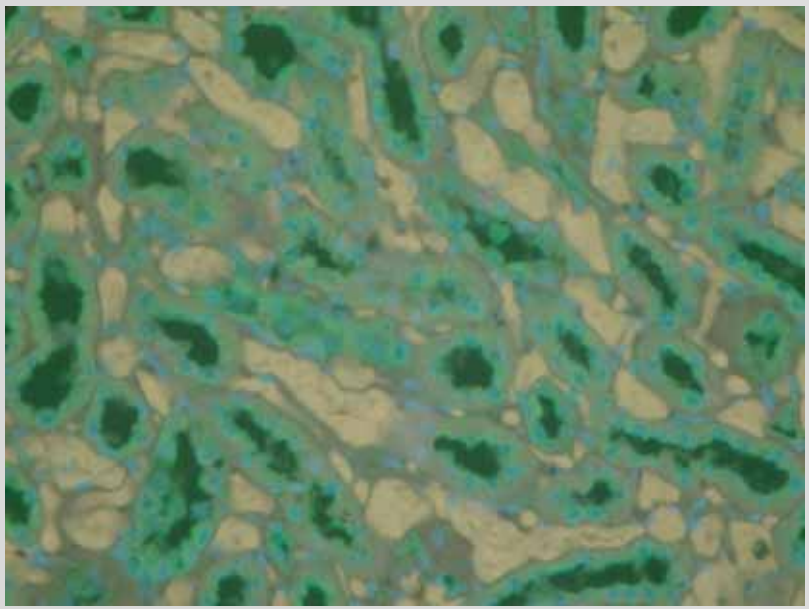
**RAGE Antibody**
**Meglumine Treated Rat**



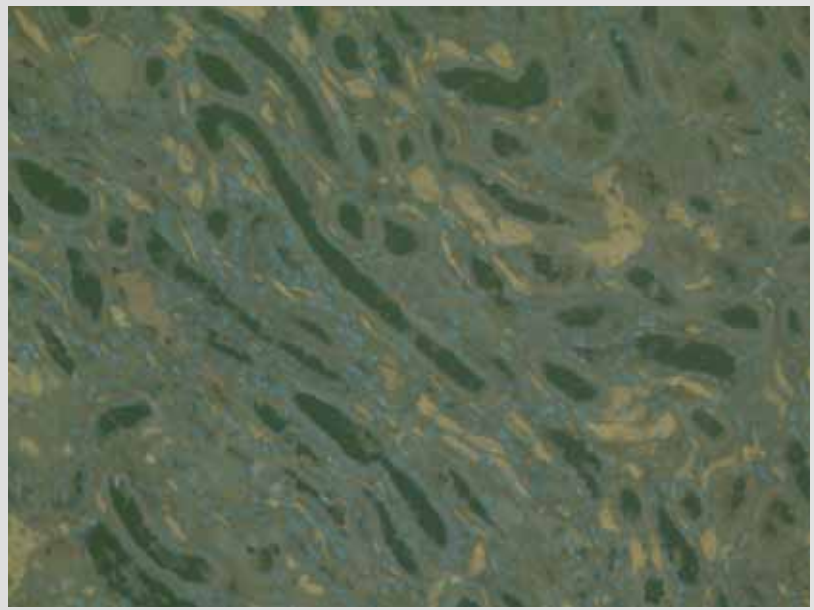
# Dynamis' Compound Controls RAGE Production in Rats Orally Dosed for 32 Weeks—Kidney Tubule

**Bright green (Florescent antibody to RAGE) indicates the presence of RAGE in the non-treated control rats vs absence of bright green in rats treated with RAGE inhibitor indicates no RAGE has formed with aging**

**RAGE Antibody**
**Control Rat**

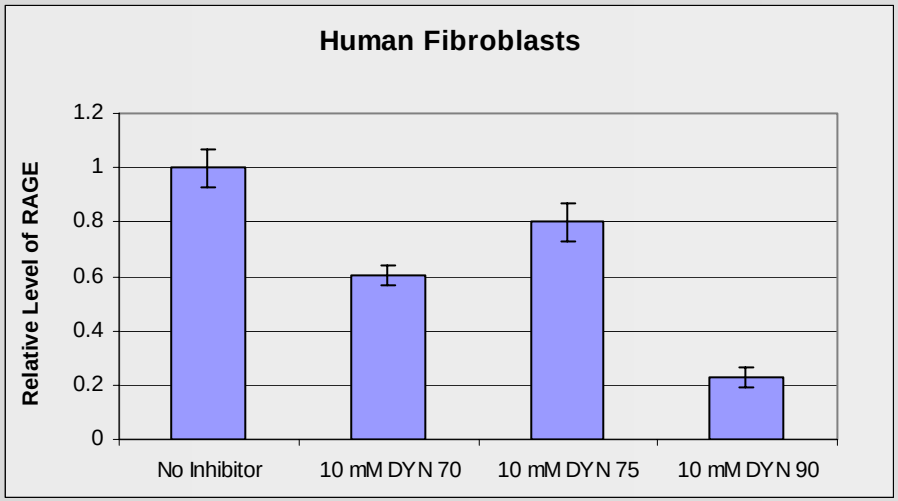


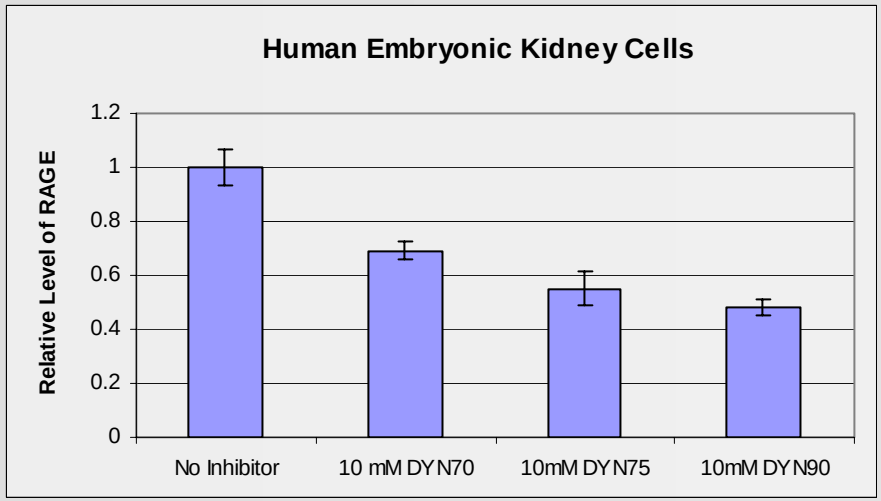
**RAGE Antibody**
**Meglumine Treated Rat**



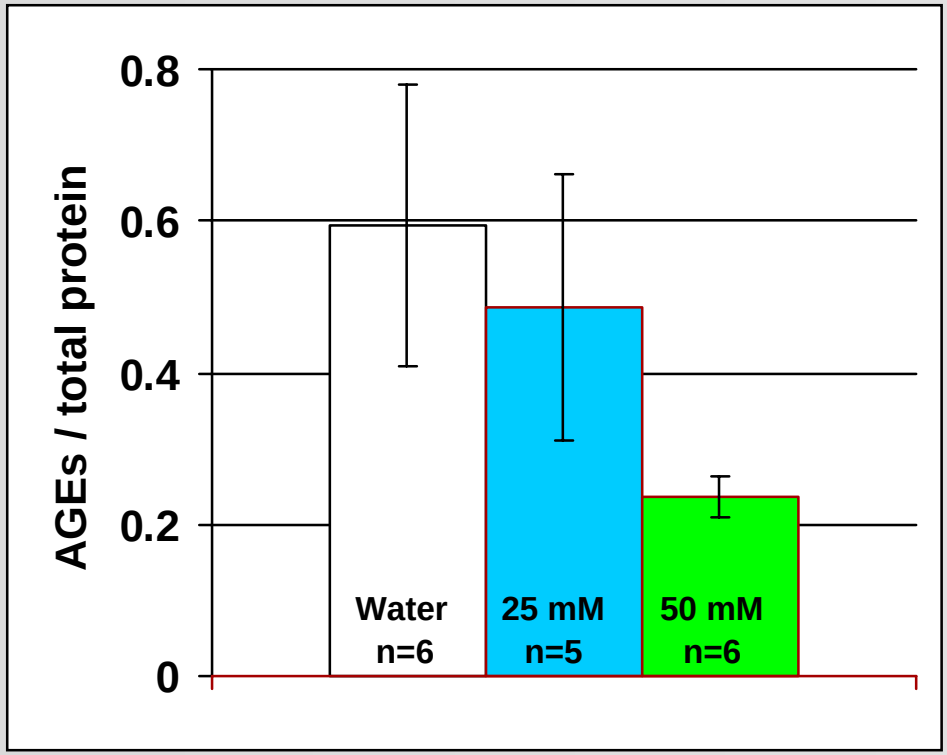
# Dynamis Inhibits Production of RAGE in Cells

**Cells were treated for 48 hr with 3 different inhibitors; RT-PCR used to quantitate RAGE.**



# Meglumine Decreases AGEs in Skin




**61% reduction in skin AGEs following oral dosing with 50mM meglumine for 32 weeks**

# *Skin Texture Study*

Before

After 21 Days

**These are pictures of a 77 year old woman taken before and after a three-week application of the cream containing *Supplamine*®.**

**The visual difference around the eye and lip areas demonstrates that the cream with *Supplamine*® reduces the appearance of fine lines.**

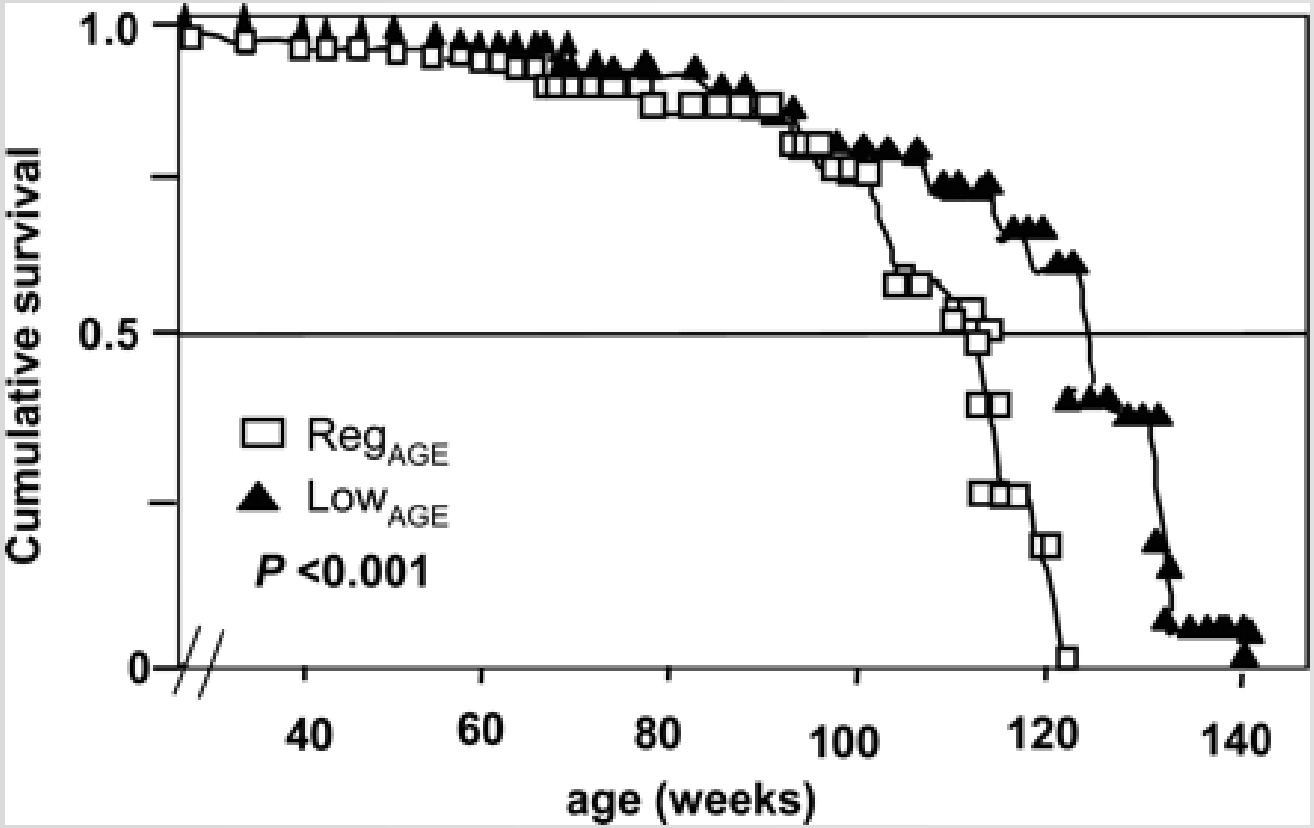
# Skin Texture Study


# *Skin Texture Study*

| *Skin Feature* * | Week 0 | | Week 4 | | Grade Change | | t-test |
|---|---|---|---|---|---|---|---|
| | Base Cream | *Supplamine®* | Base Cream | *Supplamine®* | Base Cream | *Supplamine®* | |
| Texture (Crepiness) | 5.0 | 5.0 | 4.1 | 3.7 | -0.9 | -1.3 | p = 0.032 |
| Visual Dryness | 2.9 | 2.8 | 1.8 | 1.0 | -1.1 | -1.8 | p = 0.006 |
| Tactile Dryness | 3.9 | 4.0 | 2.6 | 2.1 | -1.3 | -1.9 | p = 0.051 |

* Skin Features were graded on a scale from 0 (smooth, firm) to 8 (rough, inflexible, wrinkled).

# Low AGE Diet Results in Increased Lifespan in Mice




Cai et al., (2007) Am J Path 170:1893

# Increased Lifespan With Meglumine Given in Water

| | Days Lived | Average | % Increase |
|---|---|---|---|
| **Plain water** | 882 | 771 | |
| | 915 | | |
| | 834 | | |
| | 453 | | |
| **10mM meg** | 683 | 834 | 8.2 |
| | 782 | | |
| | 937 | | |
| | 934 | | |
| **40mM meg** | 919 | 927 | 20.2 |
| | 872 | | |
| | 1043 | | |
| | 874 | | |
| **75mM meg** | 1064 | 1027 | 33.2 |
| | 1082 | | |
| | 1109 | | |
| | 853 | | |

# Special Thanks to:

## Dynamis

*Michael Coulton*
*Frank Kappler*
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## Collaborators

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