

# ATS 2009 • San Diego

The American Thoracic Society's 105<sup>th</sup> International Conference, May 15 to 20, 2009



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## News Release

**FOR RELEASE Wednesday May 20, 2009 8:15 a.m. PDT**

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ATS Press Room: 619-525-6323, 619-525-6324 or 619-525-6325 (May 15 to 20)

Poster session time: May 20: 8:15 a.m. to 10:45 a.m.

Poster viewing time: May 20: 8:15 a.m. to 9:30 a.m.

Poster discussion time: May 20: 9:30 a.m. to 10:45 a.m.

Location: San Diego Convention Center, Room 16 A-B (Mezzanine Level)

### **Vitamin D May Halt Lung Function Decline in Asthma and COPD**

ATS 2009, SAN DIEGO—Vitamin D may slow the progressive decline in the ability to breathe that can occur in people with asthma as a result of human airway smooth muscle (HASM) proliferation, according to researchers at the University of Pennsylvania.

The group found that calcitriol, a form of vitamin D synthesized within the body, reduced growth-factor-induced HASM proliferation in cells isolated from both persons with asthma and from persons without the disease. The proliferation is a part of process called airway remodeling, which occurs in many people with asthma, and leads to reduced lung function over time.

The researchers believe that by slowing airway remodeling, they can prevent or forestall the irreversible decline in breathing that leaves many asthmatics even more vulnerable when they suffer an asthma attack.

“Calcitriol has recently earned prominence for its anti-inflammatory effects,” said Gautam Damera, Ph.D., who will present the research at the American Thoracic Society’s 105<sup>th</sup> International

Conference in San Diego on Wednesday, May 20. “But our study is the first to reveal the potent role of calcitriol in inhibiting ASM proliferation.”

The experiments were conducted with cells from 12 subjects, and the researchers compared calcitriol with dexamethasone, a corticosteroid prescribed widely for the treatment of asthma. Although, dexamethasone is also a powerful anti-inflammatory agent, the researchers found that it had little effect on HASM growth.

Dr. Damera and his colleagues found calcitriol inhibits HASM in a dose-dependent manner, with a maximum inhibitory effect of 60 percent  $\pm$  3 percent at 100nM.

As part of the University of Pennsylvania’s Airway Biology Initiative, the researchers are planning a randomized control trial of calcitriol in patients with severe asthma and expect to have data from the trial in about a year’s time.

With its anti-inflammatory qualities and its ability to inhibit smooth muscle proliferation, Dr. Damera said, calcitriol may become an important new therapy, used alone or in combination with already prescribed steroids, for treating steroid-resistant asthma.

Dr. Damera and his colleagues have also conducted experiments to determine the mechanism by which calcitriol retards HASM proliferation. They believe the vitamin works by inhibiting activation of distinct set of proteins responsible for cell-cycle progression.

The investigators have also conducted experiments to determine whether calcitriol, which is currently used to treat psoriasis, could be an effective therapy for COPD. Although preliminary, their data shows that calcitriol appears to reduce pro-inflammatory cytokine secretions in COPD. As with asthma, the researchers believe, calcitriol may also have the added benefit of slowing, if not stopping, the progression of airway remodeling. Others in the field believe calcitriol may also have the potential to inhibit the development and growth of several types of cancer.

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**Session #** D29: “Lung Remodeling: New Challenges and Promises”

**Abstract #** 2723: “Vitamin D Attenuates Growth Factor-induced Human Airway Smooth Muscle Cell Proliferation”

**Poster Board #** 509

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**Abstract Number:** 2723

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**I confirm that all authors listed on this abstract have knowledge of the abstract submission:**  
Yes

**Title:** Vitamin D Attenuates Growth Factor-Induced Human Airway Smooth Muscle Cell Proliferation

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Airway remodeling in asthma manifests by increased airway smooth muscle (ASM) mass that in part is due to myocyte proliferation. Currently, no therapeutic agents abrogate human ASM (HASM) proliferation. We hypothesize that calcitriol, a non-secosteroidal vitamin D receptor modulator, inhibits growth factor-induced myocyte proliferation. Calcitriol, but not dexamethasone, markedly inhibited PDGF-induced HASM DNA synthesis in a dose-dependent manner, with a maximum inhibitory effect of 60% ± 3% (n = 12) at 100 nM calcitriol. Calcitriol also equally inhibited HASM cell growth derived from normals or subjects with asthma. In parallel experiments, calcitriol increased expression of CYP24A1, an inducible protein dependent on vitamin D receptor activation. To determine the precise mechanism by which calcitriol inhibited growth, the effects of calcitriol on PDGF-induced p42/44 MAPK, PI3-kinase, S6kinase activation as well as cyclin D and E2F-1 expression were examined. Despite calcitriol inhibiting PDGF-induced cell growth, calcitriol had little effect on PDGF-induced activation of the aforementioned signaling pathways. In separate experiments, calcitriol treatment showed no substantial effects on HASM apoptosis as determined

by caspase 3 expression and flow cytometry. Interestingly, calcitriol markedly inhibited retinoblastoma phosphorylation as well as increased CHK-1 expression. These data suggest that calcitriol uniquely inhibits PDGF-induced HASM cell growth by inhibiting signaling pathways downstream from cyclin D expression but upstream from retinoblastoma phosphorylation. Taken together, calcitriol may offer a unique therapeutic approach in the management of diseases characterized by increased ASM mass that include asthma and COPD.