

EXHIBIT 2

(12) **United States Patent**
Dobson, Jr. et al.

(10) **Patent No.:** **US 6,645,513 B2**
(45) **Date of Patent:** ***Nov. 11, 2003**

(54) **TREATMENT OF SKIN WITH ADENOSINE OR ADENOSINE ANALOG**

(75) Inventors: **James G. Dobson, Jr.**, Auburn, MA (US); **Michael F. Ethier**, Grafton, MA (US)

(73) Assignee: **University of Massachusetts**, Boston, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **10/184,810**

(22) Filed: **Jun. 28, 2002**

(65) **Prior Publication Data**

US 2003/0044439 A1 Mar. 6, 2003

Related U.S. Application Data

(63) Continuation of application No. 09/672,348, filed on Sep. 28, 2000, now Pat. No. 6,423,327, which is a continuation of application No. 09/179,006, filed on Oct. 26, 1998, now abandoned.

(51) **Int. Cl.**⁷ **A61K 7/00**; A61K 31/7076

(52) **U.S. Cl.** **424/401**; 424/447; 424/448; 424/449; 514/46

(58) **Field of Search** 424/401, 447, 424/448, 449; 514/46

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,088,756 A	5/1978	Voorhees	424/180
4,454,122 A	6/1984	Stramentionoli et al. ...	424/180
4,839,164 A *	6/1989	Smith	424/64
5,399,349 A	3/1995	Paunescu et al.	424/195.1
5,460,959 A	10/1995	Mulligan et al.	435/172.3

5,618,544 A	4/1997	Brown	424/401
5,770,582 A *	6/1998	von Borstel et al.	514/45
5,785,978 A	7/1998	Porter et al.	424/401
5,821,237 A	10/1998	Bissett et al.	514/75
5,932,558 A	8/1999	Crostein et al.	514/46
5,998,423 A *	12/1999	Manneth et al.	514/260
6,423,327 B1 *	7/2002	Dobson, Jr. et al.	424/401

FOREIGN PATENT DOCUMENTS

DE 19545107 6/1997

OTHER PUBLICATIONS

Adair et al., "Vascular development in chick embryos: a possible role for adenosine" American Physiological Society; 0363-6135/89 1989.

Ahmed et al., "Presence of Both A₁ and A₂ Adenosine Receptors in Human Cells and Their Interaction," Biochemical and Biophysical Research Communications, 208:871-878, 1995.

Ethier et al., "Adenosine Stimulation of DNA Synthesis in Human Endothelial Cells," The American Physiological Society, 272:H1470-H1479, 1997.

Grove et al., "Optical profilometry: An objective method for quantification of facial wrinkles," Journal of the American Academy of Dermatology, 21:631-637, 1989.

Gruber et al., "Increased Adenosine Concentration in Blood From Ischemic Myocardium by AICA Riboside," Circulation, 80:1400-1411, 1989.

(List continued on next page.)

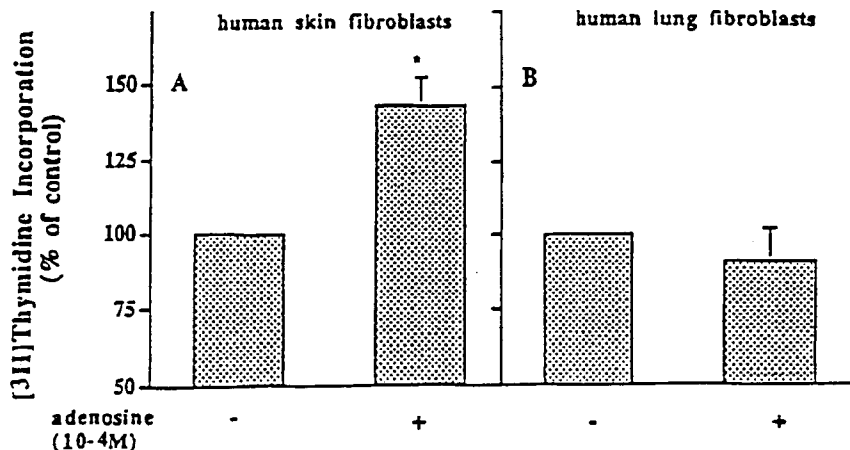
Primary Examiner—Lakshmi Channavajjala

(74) *Attorney, Agent, or Firm*—Fish & Richardson P.C.

(57) **ABSTRACT**

Methods for enhancing the condition of non-diseased skin by application of compositions containing adenosine or an adenosine analog are disclosed. Also disclosed are methods for increasing DNA synthesis or protein synthesis in dermal cells, and methods for increasing dermal cell size, by application of compositions containing adenosine.

10 Claims, 2 Drawing Sheets



OTHER PUBLICATIONS

Hartzstark et al. "The use of indentometry to study the effect of agents known to increase skin cams content" *Experientia* 41:378-379 (1985).

Kollias-Baker et al., "Agonist-independent effect of an allosteric enhancer of the A1 adenosine receptor in CHO cells stably expressing the recombinant human A1 receptor" *Journal Pharmacology and Experimental Therapeutics* 281: 761-768, 1997.

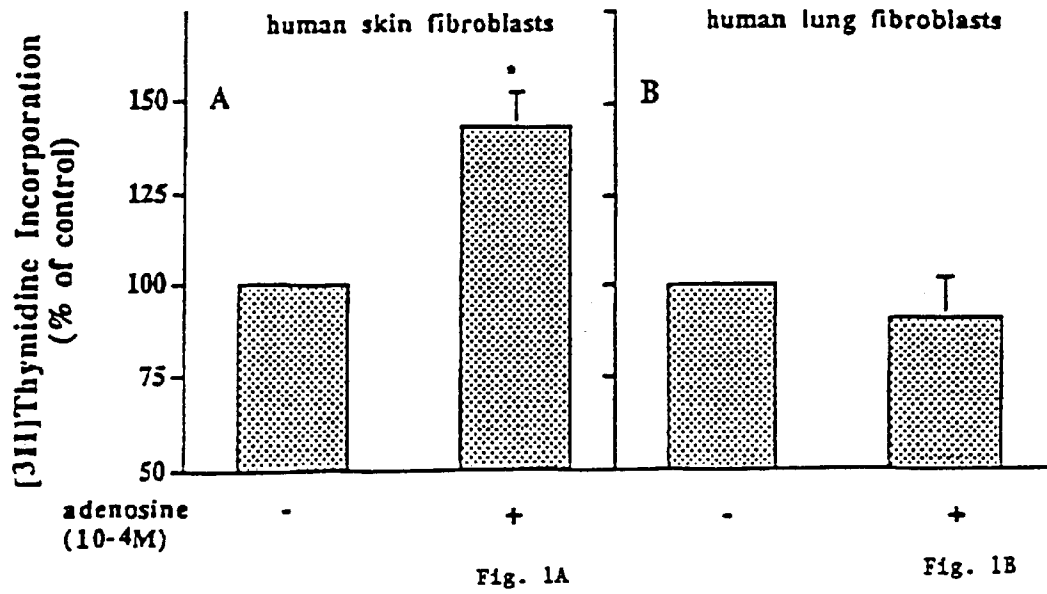
Newby et al., Critical Evaluation of the Role of Ecto—and

Cytosolic 5' Nucleotidase in Adenosine Formation Topics and Perspectives in Adenosine Research, 155-168, 1987.

Olsen et al, "Tretinoin emollient cream: a new therapy for photodamaged skin," *Journal of the American Academy of Dermatology*, 26:215-224, 1992.

Olsen et al., "Tretinoin emollient cream for photodamaged skin: Results of 48-week, multicenter, double-blind studies," *Journal of the American Academy of Dermatology*, 37:217-226, 1997.

* cited by examiner



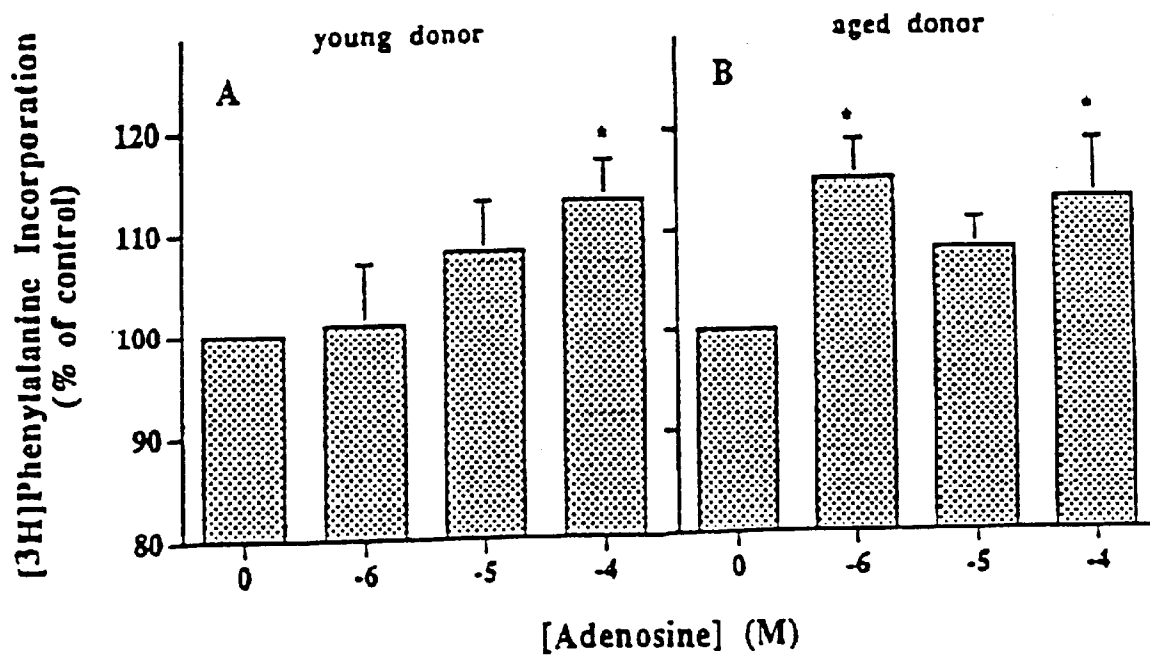


Fig. 2A

Fig. 2B

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.