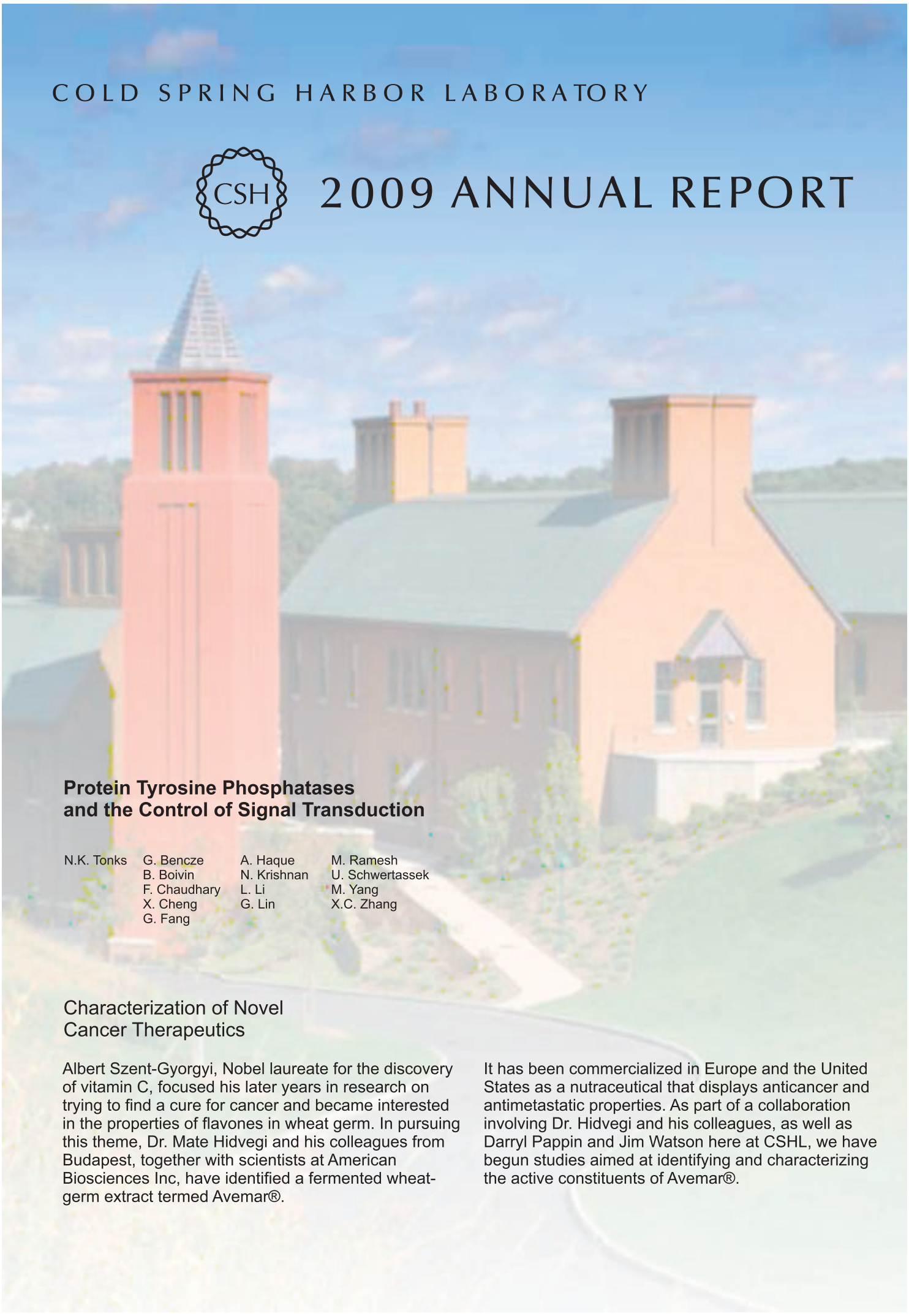
COLD SPRING HARBOR LABORATORY

2009 ANNUAL REPORT



Protein Tyrosine Phosphatases and the Control of Signal Transduction

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Characterization of Novel Cancer Therapeutics

Albert Szent-Gyorgyi, Nobel laureate for the discovery of vitamin C, focused his later years in research on trying to find a cure for cancer and became interested in the properties of flavones in wheat germ. In pursuing this theme, Dr. Mate Hidvegi and his colleagues from Budapest, together with scientists at American Biosciences Inc, have identified a fermented wheat-germ extract termed Avemar®. It has been commercialized in Europe and the United States as a nutraceutical that displays anticancer and antimetastatic properties. As part of a collaboration involving Dr. Hidvegi and his colleagues, as well as Darryl Pappin and Jim Watson here at CSHL, we have begun studies aimed at identifying and characterizing the active constituents of Avemar®.

Cold Spring Harbor Laboratory

2011 ANNUAL REPORT

Protein Tyrosine Phosphatases and the Control of Signal Transduction

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Characterization of Novel Cancer Therapeutics

Avemar® is a proprietary fermented wheat germ extract (FWGE) that has been shown to have many beneficial 100 Research characteristics, including potent anticancer, anti-inflammatory, immune-modulatory, metabolic-regulatory, cardiovascular-protective, and anti-aging properties. FWGE impairs critical aspects of the transformed phenotype, including aerobic glycolysis, the pentose phosphate pathway, and ribonucleotide reductase. It displays significant antiproliferative effects and triggers tumor cell death through apoptosis. Clinical data reveal significant benefits to patients from treatment with FWGE, including in combination with existing cancer therapies. FWGE likely comprises thousands of different molecules. In particular, it is known to contain two biologically active compounds: lectins (WGA, wheat germ agglutinin) and methoxy-substituted benzoquinones (DMBQ, 2,6-dimethoxy-p-benzoquinone; MBQ, 2-methoxybenzoquinone). Nevertheless, neither of these components are the physiologically significant active molecules of the extract. Although current data support the use of FWGE as a nonprescription nutraceutical in various cancers, it is clear that exploiting its full potential will require a more precise definition of the active ingredient core components of the mixture and the biochemical characterization of their mechanism of action. During the past couple of years, we have made considerable progress in purifying the active components of Avemar®, using procedures that are readily adaptable to large-scale production. Various fractions from the initial purification procedure have been screened in cell viability assays on a broad panel of tumor cell lines and animal models, with encouraging results. In an important first step, a fraction has been generated, termed A250, which represents ~3% of the dry weight of Avemar®, yet retains essentially all of the activity, and has the potential to represent a new product. In collaboration with Darryl Pappin and Jim Watson here at CSHL and Mate Hidvegi and his colleagues from Budapest, we are now focusing on producing stable, enriched, and well-characterized fraction(s) from crude FWGE that show significant activity in cell and animal models of cancer, with the goal of developing novel therapeutics.

Cold Spring Harbor Laboratory

2012 ANNUAL REPORT

Protein Tyrosine Phosphatases and the Control of Signal Transduction

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Characterization of Novel Kinase Inhibitors

In collaboration with Drs. Darryl Pappin and Jim Watson here at CSHL and Mate Hidvegi and his colleagues from Budapest, this lab led a project to identify the active components of Avemar®, a proprietary fermented wheat germ extract (FWGE) nutraceutical that has been shown to display signifi cant antiproliferative effects and to trigger tumor cell death through apoptosis. Clinical data reveal significant benefits to patients from treatment with FWGE, including in combination with existing cancer therapies. Through this collaboration, a novel small-molecule protein kinase inhibitor (CSH-4044) has now been isolated from FWGE and characterized. This inhibitor has both a unique structure and a unique specificity for PIM (proviral integration site for Moloney murine leukemia virus) and DYRK (dual specificity tyrosine-regulated kinase) when assayed against a panel of 140 distinct protein kinases. Current efforts are focused on testing this inhibitor in appropriate cancer models and optimizing its structure, both to enhance potency, specificity, and bioavailability, as well as to improve drug-like characteristics. In collaboration with Dave Tuveson, CSH-4044 is being tested in cell and animal models of pancreatic cancer, using inhibition of PIM and DYRK as a new approach to inhibiting signaling downstream of KRAS. In addition, it is being tested in collaboration with Chris Vakoc in his leukemia models. It is anticipated that this study will validate a novel therapeutic candidate for treatment of these cancers.

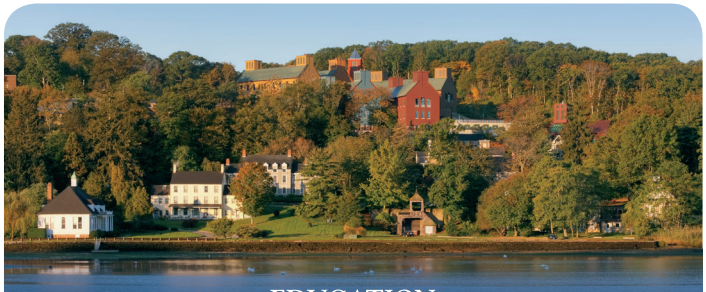
Cold Spring Harbor Laboratory

Founded in 1890, Cold Spring Harbor Laboratory (CSHL) is a preeminent international research institution, achieving breakthroughs in molecular biology and genetics and enhancing scientific knowledge worldwide.

RESEARCH

United by the goal of alleviating major causes of human suffering, CSHLs 600 researchers and technicians focus on:

- Cancer
- Neuroscience
- Genomics
- Quantitative Biology
- Plant Biology



EDUCATION

CSHL is recognized as a pioneer in science education, training professional scientists, students and teachers:

Watson School of Biological Sciences: trains the next generation of scientists through an innovative Ph.D. program that fully funds the doctoral research of each student.

Meetings & Courses Program: attracts 12,000 scientists annually from around the world to learn the latest technologies and share advances in biological research.

Banbury Center: a think-tank that convenes global experts to guide science and public policy.

DNA Learning Center: produces web-based multimedia tools, delivers hands-on learning experiences to 30,000 middle and high school students every year, and trains teachers; over 420,000 students have been taught in N.Y. state alone.

CSHL Press: publishes authoritative materials for the global scientific community, with journals, books and manuals used in over 2,000 academic institutions worldwide.

CSHL ranked #1 in the world for impact in molecular biology and genetics.

Top Institutions in Molecular Biology and Genetics

Published and cited between January 2002 and December 2012

	Institution	Citations per paper
1	Cold Spring Harbor Laboratory	96.94
2	MIT	87.82
3	Salk Institute for Biological Studies	70.85
4	Wellcome Trust Sanger Institute	70.27
5	Massachusetts General Hospital	67.50
6	Rockefeller University	62.46
7	Dana Farber Cancer Institute	62.22
8	European Molecular Biology Laboratory	59.41
9	Brigham and Womens Hospital	59.03
10	Memorial Sloan-Kettering Cancer Center	58.16

THOMSON REUTERS

FACTS & FIGURES

Home to eight Nobel laureates, including James D. Watson, co-discoverer of the DNA double helix.

National Cancer Institute-designated Cancer Center for over 25 years.

Incubator for more than 20 biotechnology start-ups.

Highest rating from Charity Navigator.

BY THE NUMBERS

Annual Operating Budget	$150 million
Endowment	$320 million
Research laboratories	52
Postdoctoral fellows	160
Graduate students	125
Total employees & students	1200
Annual Meetings & Courses attendees	12,000
Annual DNA Learning Center students	30,000

Updated March 2013