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## Scientific Summary

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5. List of scientific publications
6. Ask a Doctor (FAQ)
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## ImmunExtra® with Proligna® PPC

Frank Tufaro, Ph.D.

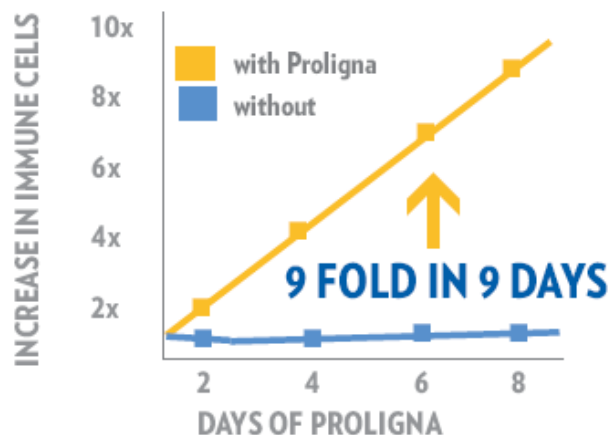
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There are now more than 30 peer-reviewed scientific studies describing research with PROLIGNA® (also known as PPC in the scientific literature). In these studies, PPC exhibits antibacterial, antiviral, and antitumor properties. Moreover, extensive experimentation shows that PPC has a positive and lasting effect on human immune cell activity at the dosage contained in ImmunExtra® capsules.

### 1. PROLIGNA EFFECTS ON IMMUNE CELLS

Proligna® PPC promotes immune cell development in human cells and animal models. In 2003, Dr. Guy Bradley demonstrated that PPC is capable of promoting the rapid differentiation of human peripheral blood mononuclear cells (PBMC) into mature **dendritic cells**.

**Proligna® contained in ImmunExtra® promotes immune cell development**



Bradley et. al., 2003 (Int. Immunopharmacology 3:209)

This is important because dendritic cells are recognized as one of the most important cells for the development of immune responses against bacterial- and viral-infected cells, cancer cells and vaccine antigens.

## **2. PPC EFFECTS ON BACTERIA AND VIRUSES**

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Dr. Satoh's laboratory (Satoh et. al., 1999) showed that PPC inhibits HIV induced effects on cells in cell culture. Moreover, pretreatment of mice with PPC by injection protects them from a lethal infection with E. coli bacteria. These results support the potential benefits of PPC.

## **3. PPC EFFECTS ON TUMOR RESPONSE TO CHEMOTHERAPY<sup>2</sup>**

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Dr. Mark Jaroszeski's laboratory at the University of South Florida investigated the potential beneficial effects of PROLIGNA<sup>®</sup> (PPC) when used in conjunction with a procedure called electrochemotherapy (ECT) for the treatment of tumors.

ECT involves applying electrical pulses to living cells, which cause the rapid appearance and disappearance of tiny holes in the cell membrane. This procedure allows chemotherapy drugs to

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<sup>2</sup> Dr. Mark J. Jaroszeski et. al, (2006) Abstract to the American Institute of Chemical Engineers Annual meeting. This work was supported by Grant Number R21AT001259 from the National Institutes of Health (NIH), National Center for Complimentary and Alternative Medicine (NCCAM).

enter the cells more efficiently. ECT has been exploited to deliver chemotherapeutic agents to tumor cells in clinical trials in the US and Europe.

The current study tested ECT plus **Proligna** (PPC) in an animal model for melanoma, a particularly aggressive cancer type.

Treatment "success" was defined as the complete absence of tumor at the end of 50 days. Remarkably, 50 to 64% of the animals that received oral PPC plus ECT had a complete absence of tumor versus 31% for animals that received ECT alone. It was concluded that treatment of animals with PPC caused a doubling of the number of animals that were tumor free during the course of the experiment.

Additional studies will need to be done to sort out the precise basis for these interesting results.

## **4. THE SAFETY OF PPC**

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Toxicology experiments have proved that Proligna PPC is non-toxic when taken orally for 30 days at a range of dose levels (5 mg/kg up to 405 mg/kg)<sup>3</sup>. Studies performed in mice further support these results. Moreover, more than a million doses of pinecone extract have been distributed to people with no apparent side effects.

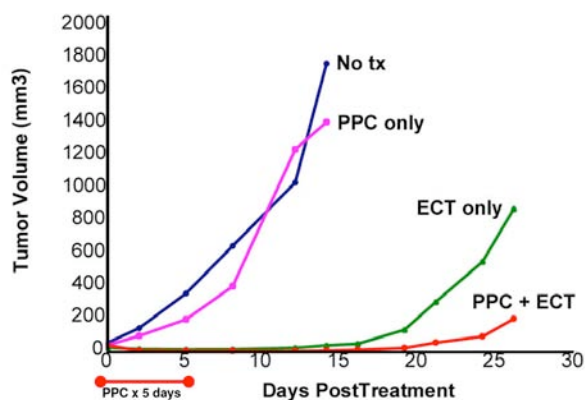
In summary, all of these study results suggest that pinecone extract could be useful for maintaining health without associated side effects.

For complete results, please see publications listed in the next section.

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<sup>3</sup> Performed in a rat model

## Proligna + Chemotherapy (PPC+ECT) is Superior to Chemotherapy (ECT) Alone for Killing Melanoma Tumors in Mice



## 5. SCIENTIFIC PUBLICATIONS ON PPC

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### Antimicrobial effects

1. Harada *et. al.*, (1988) Induction of antimicrobial activity by antitumor substances from pinecone extract of *Pinus parviflora* Sieb. et Zucc. *Anticancer Research*. 8:581-588.
2. Oh-hara *et. al.*, (1990) Antimicrobial spectrum of lignin-related pinecone extracts of *Pinus parviflora* Sieb. et Zucc. (1990) *In vivo*. 4: 7-12.

### Antiparasitic effects

1. Abe *et. al.*, (1989) Induction of antiparasitic activity by pinecone lignin-related substances. *In vivo*. 3:359-362.

### Antitumor/antiviral effects

1. Mark J. Jaroszeski<sup>1</sup>, Richard Heller<sup>2</sup>, Anna Claire Johnson<sup>3</sup>, Kathleen Merkler<sup>2</sup>, Akiko Tanaka<sup>4</sup>, and William Guy Bradley<sup>5</sup>. (2006) Extract of Pinecones Augments Tumor Response to Electrochemotherapy. Abstract. 2006 AICHE Annual Meeting.
2. Kikuchi *et. al.*, (1991) Stimulation of mouse peritoneal macrophages by lignin-related substances. *Anticancer Research*. 11:841-846.
3. Nagasawa *et. al.*, (1992) Inhibitory effect of lignin-related pinecone extract on cell proliferating enzyme activity of spontaneous mammary tumors in mice. *Anticancer Research*. 12: 501-504.
4. Nagasawa *et. al.*, (1992) Suppression by a pinecone extract of *Pinus parviflora* Sieb. et Zucc of mammary tumor virus in milk of mice. *Anticancer Research*. 12: 845-848.
5. Unten *et. al.* (1989) Stimulation of granulocyte cell iodination by pinecone antitumor substances. *Journal of Leukocyte Biology*. 45: 168-175.

## **Cytotoxic/mitogenic effects**

1. Kawazoe *et. al.*, (1993) Mechanism of splenocyte-mitogenesis induced in mice by water-extract of coniferous slash pine. *Anticancer Research*. 13: 1223-1230.
2. Kurakata *et. al.*, (1989) Mitogenic activity of pinecone extracts against cultured splenocytes from normal and tumor-bearing animals. *Anticancer Research*. 9: 961-966.
3. Sakagami *et. al.*, (1990) Induction of cytotoxic factor in mice by lignified materials combined with OK-42 (Picibanil). *In vivo*. 4: 371-376.

## **Immune modulating effects**

1. Bradley *et. al.*, (2003) The novel differentiation of human blood mononuclear cells into CD 1a negative dendritic cells is stimulated in the absence of exogenous cytokines by an extract prepared from pinecones. *International Immunopharmacology*. 3: 209-223.
2. Eberhardt and Young (1996) Assessment of anti-viral activity of a pinecone isolate. *Planta Medica*. 62: 63-65.
3. Fukuchi *et. al.*, (1989) Inhibition of *Herpes simplex* virus infection by pinecone antitumor substances. *Anticancer Research*. 9: 313-318
4. Kunisada *et. al.*, (1992) Effect of lignins on HIV-induced cytopathogenicity and myeloperoxidase activity in human myelogenous leukemic cell lines. *Anticancer Research*. 12: 2225-2228.
5. Lai *et. al.*, (1990) Modification of HIV replication by pinecone extracts. *AIDS Research and Human Retroviruses*. 6(2): 205-217.
6. Lai *et. al.*, (1992) Polymeric phenylpropenoids are the active components in the pinecone extract that inhibit the replication of type-1 HIV *in vitro*. *Journal of General and Applied Microbiology*. 38: 303-312.
7. Sakagami *et. al.*, (1986) Partial purification of novel differentiation-inducing substances from hot water extract of Japanese pinecone. *Japanese Journal of Cancer Research*. 77: 59-64.
8. Sakagami *et. al.*, (1990) Anti-Influenza virus activity of synthetically polymerized phenylpropenoids. *Biochemical and Biophysical Research Communications*. 172 (3): 1267-1272.
9. Sakagami *et. al.*, (1992) Multiple immunological functions of extracts from the cone of Japanese white pine, *Pinus parviflora* Sieb. et Zucc. *Microbial Infections*. Ed. H. Friedman *et. al.*, 331-335.
10. Satoh *et. al.*, (1999) Radical modulation activity of pinecone extracts of *Pinus elliottii* var. *Elliottii*. *Anticancer Research*. 19: 357-364.
11. Takayama *et. al.*, (1991) Inhibition of HIV forward and reverse transcription by PC6, a natural product from cones of pine trees. *AIDS Research and Human Retroviruses*. 7(3): 349-357.
12. Tamura *et. al.*, (1991) A soluble factor induced by an extract from *Pinus parviflora* Sieb. et Zucc can inhibit the replication of HIV *in vitro*. *Proceedings of the National Academy of Science*. 88: 2249-2253.

## **6. ASK A DOCTOR (FAQ)**

**Dr. Joanna J. Peterkin, M.D., M.S.**

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### **How can I help my immune system?**

Various factors can stress your immune system. Smoking, poor eating habits, unhealthy diets, excessive alcohol, lack of exercise, lack of sleep and anxiety all affect how your body will fight off invaders and recover from illness.

All of us come in contact with harmful bacteria, viruses and other pathogens at some point during our life, if not on a daily basis. Fortifying and maintaining your immune system by leading a healthy lifestyle and making healthy choices will reduce susceptibility to infection and other diseases while augmenting your body's ability to protect itself.

Try these 4 simple tasks to help your body protect and heal itself:

1. Regular exercise will help reduce daily stress while physically strengthening your body and improving general well being.
2. Getting enough rest so your body has time to defend itself will also reinforce the health of your immune system.
3. To further optimize immune system function, minimize your intake of sugar, saturated fat and alcohol and exchange it for minerals and nutrients .
4. Finally, supplementing your diet with ImmunExtra® can positively impact the response and performance of your immune system.

### **How is ImmunExtra® different from other immune health products?**

ImmunExtra® is the only dietary supplement based on the patented Proligna PPC compound. Many immune health products on the market are simply a combination of ingredients, such as echinacea and vitamin C. By contrast, ImmunExtra contains a single active ingredient.

Scientists have studied PPC for more than 20 years. Proligna PPC has been shown to have a positive and lasting effect on human immune cell activity at the dose contained in ImmunExtra capsules.

### **Does ImmunExtra® cause any side effects?**

There has been more than 20 years of human experience with pinecone extract in the U.S. To date, there have been no known associated or reported side effects or adverse reactions. In addition, pinecone extract has been used for medicinal purposes for centuries.

### **What is in ImmunExtra®?**

Each capsule of ImmunExtra contains the active ingredient Proligna. There is a small amount of vegetable extract required for making a vegetarian capsule. ImmunExtra® does not contain any animal products, yeast, dairy, eggs, gluten, soy, wheat, peanuts, tree nuts, fish, shellfish, or any artificial ingredients. The pinecones from which the botanical compound is extracted are harvested in the forests of Wisconsin and Minnesota. They are a renewable resource.

Allera adheres to Food GMPs and the regulations of the Dietary Supplement Health Education Act of 1994 (DSHEA) for the product. The provisions of DSHEA define dietary supplements and dietary ingredients; establish a new framework for assuring safety; outline guidelines for literature displayed where supplements are sold; provide for use of claims and nutritional support statements; require ingredient and nutrition labeling; and grant the FDA the authority to establish Good Manufacturing Practice regulations. Any advertising claims made about Immunextra® are subject to regulation by the U.S. Federal Trade Commission (FTC).

### **What are some of the conditions for which ImmunExtra® may help?**

Double blind, placebo-controlled clinical studies are currently underway to investigate the effectiveness of ImmunExtra for osteoarthritis. Users have reported anti-inflammatory benefits as well as generally feeling better after taking ImmunExtra daily.

### **How many capsules of ImmunExtra® should I take and how often?**

The recommended effective dose is one or two capsules every day. It does not matter if you take the capsules in the morning, afternoon or evening.

### **Should I take ImmunExtra® with food?**

The food you eat or the dietary supplements you take could cause a medication you are taking to work incorrectly. When supplements or drugs and certain foods are taken together they can interact in ways that can diminish or intensify the effectiveness of the drug or reduce the absorption of food nutrients. In addition, vitamin and herbal

supplements taken with certain medications can result in adverse effects. For example, food can speed up or slow down the action of a medication or supplement, while certain drugs can change how nutrients are used or decrease the absorption of vitamins and minerals in the body, or stimulate or suppress the appetite, and certain herbs can interact with anesthesia, beta-blockers, and anticoagulants.

The impact of food-drug and food-supplement interactions can depend on a variety of factors such as the dose, age, weight and health of the person, and the timing of when food is eaten and when a medication or supplement is taken.

Avoiding interactions does not necessarily mean not taking supplements or drugs and not eating foods. In the case of tetracycline and dairy products, each should simply be taken at a different time rather than eliminating one or the other.

There are no known interactions of ImmunExtra® and food. ImmunExtra® can be taken with food and liquids or without.

### **Can I take ImmunExtra® with other medications and/or dietary supplements?**

There have been no reported contraindications for ImmunExtra when taken together with other medicines or dietary supplements including vitamins.

### **Can children take ImmunExtra?**

On the basis of prior experience, children can take ImmunExtra® at a recommended dose of one capsule a day.

### **Can I take ImmunExtra if I'm pregnant?**

There have been no formal clinical studies conducted with women who are pregnant. If you are pregnant or trying to become pregnant, you should not take ImmunExtra® since there is no information regarding any effects it may have on an unborn baby. This is true for all dietary supplements and many drugs. It is always best to consult with your doctor before taking a new supplement, medicine, or product especially if you are pregnant.

### **What happens if I take too many capsules of ImmunExtra®?**

There is no information on the effects of overdose or taking too many capsules of ImmunExtra. No safety concerns have been reported over the many years ImmunExtra and pinecone extract have been used. Formal clinical trials with ImmunExtra are underway in the United States to evaluate product safety and efficacy in a standard manner. Consult with your doctor if you have any concerns.

## 7. ALLERA MANAGEMENT TEAM

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### Directors, Officers and Key Employees and Consultants

The directors, officers and key employees of the Company are as follows:

<u>Name</u>	<u>Position</u>
<b>Francis Tufaro, Ph.D.</b>	<b>Chief Executive Officer, Director</b>
<b>Eddy Kelly</b>	<b>Chairman-Board of Directors</b>
<b>G. Kristin Delano</b>	<b>Director</b>
<b>Anthony Guglielmin</b>	<b>Director</b>

### Management

<b>Frank Tufaro, Ph.D.</b>	<b>President and Chief Executive Officer</b>
<b>John Miller</b>	<b>Branding and Website</b>
<b>Ofelia Barretto, M.S.</b>	<b>Quality Assurance</b>
<b>Erin Mitchell, Ph.D.</b>	<b>Manufacturing</b>

### Management Team

#### **Frank Tufaro, Ph.D., President and CEO**

Frank Tufaro received his B.Sc. and Ph.D. in Molecular Biology from McGill University in Montreal, Canada. He subsequently carried out postdoctoral research at the Fred Hutchinson Cancer Research Center (Seattle, WA) and The Carnegie Institution of Washington (Baltimore, MD) with Dr. Steve McKnight. Frank went on to a successful career at the University of British Columbia Department of Microbiology, where he was a full professor with expertise in Virology and Cancer.

Frank has experience with biotechnology firms. He was one of the original founders of Neurovir, Inc., a Vancouver-based biotech Company with a mission to develop herpes-simplex virus oncolytic vectors for treating cancer. Frank initially served as Chief Scientific Officer, where he managed all aspects of drug development, including FDA interactions and contract manufacturing. He then served as CEO.

Frank remains active in both the business and scientific arenas. He recently served on the Canadian Institutes of Health Research Viral Pathogenesis grant panel, and currently

serves on the Scientific and Executive Advisory Boards of several biotechnology companies, both public and private.

### **John Miller, Branding and Web Marketing**

John Miller has worked in print media for more than 20 years as an art director and editor at numerous publications, including Vanity Fair, HarperCollins and Esquire. He has consulted on redesigns of many newspapers and magazines, among them The Wall Street Journal, Forbes, and The Los Angeles Times. Since 1994, he has developed web sites for MSNBC, Bank of America, Amazon, Intel, Target, The National Park Service, The Department of Defense, and many others.

### **Ofelia U. Barretto, Quality Assurance**

Ofelia is a quality professional with more than 40 years experience in the management of quality assurance/control of drugs, pharmaceuticals, cosmetics, foods, and nutritional supplements. She has authored and presented papers, nationally and internationally, on quality systems, supplier quality management, GMPs, HACCP, auditing, preparing for an FDA inspection, international harmonization of standards, and ISO 9000 / GMP concepts. She is an international trainer on GMPs, an AFDO certified trainer on HACCP and Sanitation Control Procedures (SCP), and a trainer on Quality Management Systems for the Southern California Food Industry Roundtable (FIBR). She is a guest lecturer at California State University, Long Beach. She conducts in-house training courses on the different GMPs, HACCP, SCP, ISO 9000-2000, and QMS. She recently authored the Edison/FIBR Food GMP Manual that incorporates the requirements of GMPs, HACCP and SCP, in a Quality Management Systems approach.

Ofelia is the President of the American Society for Quality (ASQ), a National Director in 1997-99, Chair for the Food, Drug and Cosmetic (FDC) Division in 1995-1996, and is the current FDC Conference Chair. She also chairs the annual West Coast Conference co-sponsored with the US FDA and California FDB. She has received several Awards from the Society and the Division, the latest of which was the Mae Tarber-Goodwin Award for Excellence in a Technical Publication, the Edison/FIBR Food GMP Manual.

For her activities in the GRP Partnership, Ofelia received the Hammer Award from the Office of Vice President Al Gore in 1997, and in May 1998, she received the US FDA Commissioner's Special Citation "For outstanding leadership and commitment in furthering FDA's efforts to provide the consumer and the regulated industry with a more responsive Agency."

In December, 2003, Ofelia was presented a Certificate of Appreciation from the City of Los Angeles by Mayor James K. Hahn, and an Award of Merit from the County of Los Angeles by Supervisor Yvonne Brathwaite Burke, for her involvement as a trainer for the FIBR Safety and Quality Management Systems Institute.

Ofelia has a Bachelor of Science in Chemistry (MS equivalent) and a Master in Business Administration. She retired from her position as Director of Quality Assurance for Nutrilite Division, Amway Corporation, and is now the President of Compliant Quality Solutions, a consulting firm specializing in GMP and HACCP compliant Quality Management Systems.

### **Erin Mitchell, Ph.D.**

Dr. Mitchell is the former Associate Director of Manufacturing for Neurovir, Inc. and MediGene, Inc., where she directed the manufacturing of pharmaceutical grade herpesvirus for the treatment of brain tumors. Erin is highly experienced in managing complex projects at contract manufacturing organizations such as those used by the Company. She received her Ph.D. from the Division of Immunology, University of Cambridge, Cambridge, UK, and a Masters of Science from the University of Toronto, Toronto, Canada.

### **Allera Scientific Advisory Committee**

The Tampa Bay Research Institute is an independent 501(c)(3) not for profit organization dedicated to the study, cure, and prevention of cancer and infectious diseases. The TBRI Scientific Advisory Board, composed of practicing clinicians and experts in several key areas of the Company's therapeutic focus and research, are also members of the Allera Scientific Steering Committee.

Scientists at the Tampa Bay Research Institute continue to work independently on PPC technology. Dr. Tanaka, a founder of TBRI, is a key inventor in this space and remains a driving force at the Institute. Dr. Guy Bradley, an expert in virology, worked with Dr. Akiko Tanaka on the structure and activity of PPC that resulted in patents.

Allera Health Products, Inc. is not an affiliate of the Tampa Bay Research Institute.

### **Scientific Advisory Board**

In addition to the management team, the Company has assembled a Scientific Advisory Board ("SAB") composed of practicing clinicians and experts in several key areas of the Company's therapeutic focus and research.

### **Richard Whitley, M.D.**

Dr. Whitley is Professor of Pediatrics, Microbiology and Medicine; Loeb Scholar in Pediatrics; Director, Division of Pediatric Infectious Diseases; Vice-Chair, Department of Pediatrics; Senior Scientist, Department of Gene Therapy; Senior Scientist, Cancer Research and Training Center; Associate Director for Clinical Studies, Center for AIDS Research; Director, Center for Biodefense and Emerging Infections. The University of Alabama at Birmingham. Dr. Whitley is responsible for the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group whose role is to perform clinical trials of antiviral therapies directed against medically important viral diseases of children and adults including viruses considered as threats to human health. Dr. Whitley's other research interest is in the translation of molecular biology to clinical application, particularly in the development of human monoclonal antibodies for therapy of herpesvirus infections and engineering of herpes simplex virus for gene therapy. In these latter studies, he and his colleagues have engineered herpes simplex virus to serve as a vector for foreign

gene expression. These viruses have been advanced into human treatment studies of glioblastoma multiforme.

He received his B.A. in chemistry from Duke University and his M.D. from the George Washington University. He subsequently completed an internship in pediatrics and a fellowship in infectious diseases/virology at the University of Alabama at Birmingham. He has published over 260 articles. He serves on numerous government advisory committees, including VERBAC and the Board of Scientific Councilors for NIAID. Dr. Whitley is a member of MediGene's and Gilead's Scientific Advisory Board, and formerly served on the Scientific Advisory Board of NeuroVir Therapeutics and MediGene AG.

#### **G. Yancey Gillespie, Ph.D.**

Dr. Gillespie obtained B.A. (biology & chemistry), M.Sc. (cytogenetics) and Ph.D. (immunology & immunogenetics) degrees at the University of Mississippi, finishing in 1971. Following a NCI postdoctoral fellowship at the University of Kansas Medical Center, he joined the Department of Pathology. In 1975, he joined Scripps Clinic and Research Foundation in La Jolla. In 1977, he moved as Assistant Professor of Pathology to the University of North Carolina-Chapel Hill. In 1977, he transferred to the Department of Surgery, Division of Neurosurgery to direct the Brain Tumor Immunology research program. In 1986, Dr. Gillespie came to UAB as tenured Associate Professor of Surgery to direct brain tumor research efforts in the Division of Neurosurgery. He is Professor of Surgery with secondary appointments in Departments of Microbiology and Cell Biology. Dr. Gillespie is co-Director of the UAB Brain Tumor SPORE, and leader of Brain Tumor Tissue and Brain Tumor Animal Models Core Facilities.

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