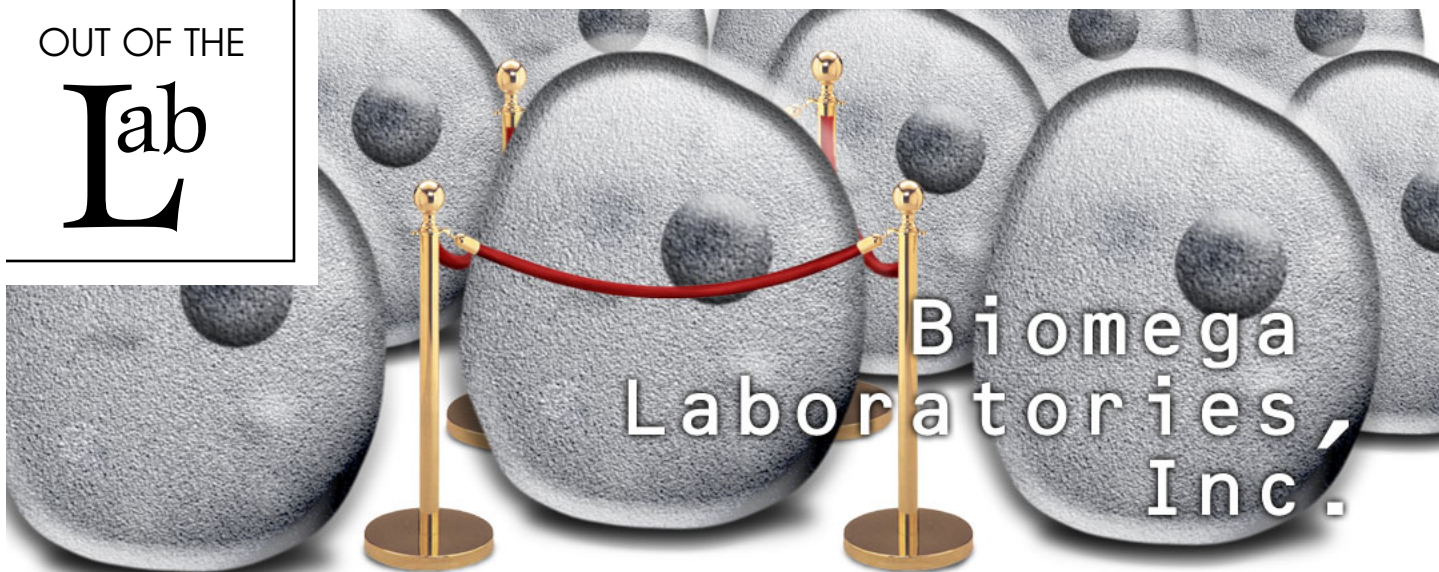


OUT OF THE  
**L**ab



**Biomega Laboratories, Inc.**

In the summer of 1966 the Beach Boys and the Beatles topped the popular music charts, the now classic television show Star Trek first aired, and a young physician-scientist by the name of George Lipkin filed for an National Cancer Institute grant to study melanoma. He held the belief that melanoma could actually be a reversible disease. This was considered quite a radical idea at that time and Dr. Lipkin had never received his own grant before. Nevertheless, the grant was awarded and a lifelong pursuit was underway. This work became the foundation of Biomega Laboratories, Inc. ("Biomega"), a company devoted to development of a substance that might just make that original idea a reality.

Not a lot was known at that time about the biological characteristics that distinguished cancer from normal cells. Dr. Lipkin began by transfecting hamster melanoma cells (melanoma is malignancy in the

pigment producing cells of the skin) with DNA or RNA from blue nevi. Blue nevi are heavily pigmented, benign cells that most people would recognize as birthmarks. Although the next three years were mainly spent optimizing the methods for transfection of the DNA or RNA, the results seemed to justify the effort. Dr. Lipkin was able to reintroduce pigmentation to non-pigmented melanoma cells. Even more encouraging, these same cells displayed a 400 % decrease in their growth rate, making them more like normal skin cells. He also discovered melanoma cells that did not reacquire the ability to produce pigmentation but behaved like normal melanocytes in another very important way.

Normal cells exhibit contact inhibition - they cease to grow or divide any further once they encounter another cell. Malignant cells no longer display this behavior. Fortuitously, during one transfection experiment, Dr. Lipkin came upon a non-pigmented cell line that

continued to display contact inhibition. These new cells became the subject of his studies for the next several years, but they failed to reveal the agent conferring contact inhibition. However, a breakthrough would occur during a sabbatical in Switzerland.

While working in a laboratory at the Abteilung für Krebsforschung, in Zurich, Dr. Lipkin decided to try something very different. He took a sample of the medium that bathed this new cell line and added it to a fresh culture of hamster malignant melanoma cells. Within 48 hours these cells also began to exhibit contact inhibition and more normal growth. What he had witnessed was the passive transfer of contact inhibition by an unknown element found in the media of the transfected hamster melanoma cells. This element was named "Contact Inhibitory Factor", or "CIF™". Upon exposure to hamster cell-derived CIF, contact inhibition and "normalization of growth" was also apparent in a wide

variety of human, mouse and rat cancer cell lines including melanoma, colon carcinoma, neuroblastoma, neurinoma, glioma, mammary carcinoma, rhabdomyosarcoma, prostate carcinoma, lung carcinoma, and several other solid tumors.

Upon his return from Zurich Dr. Lipkin, then joined by Dr. Martin Rosenberg, conducted further *in vitro* experiments. They demonstrated that CIF restores the three main analogues of normal *in vivo* growth to cancer cells. In addition to density dependent growth, or contact inhibition, the cells also displayed serum dependent growth and anchorage dependent growth. Microscopic examination of the CIF treated cells revealed a more normal appearing cytoskeleton,

important for normal cell signaling and growth regulation.

In order to determine CIF's effectiveness *in vivo*, hamster melanomas were implanted subcutaneously into hamsters and a formulation of partially purified CIF injected twice weekly around the tumor. Despite the termination of treatment after 30 days, the tumors began to recede, eventually disappearing. While all of the control hamsters perished by week 9 with massive tumors, the CIF-treated hamsters lived full life spans with no evidence of cancer. Pathology showed only the presence of necrotic tissue where the tumor had been with no evidence of overt local or systemic toxicity.

A similar experiment done in

mice with implanted Lewis lung carcinoma led to regression in 75% of tumors after only 10 days of CIF treatment. Only fluid and necrotic debris remained at the site of the tumors.

These *in vitro* and *in vivo* experiments suggested that Dr. Lipkin had discovered an endogenous and apparently non-toxic factor that restores normal growth controls to cancer cells and causes permanent regression of tumors. Furthermore, its effects were neither species nor tissue specific. His focus then turned towards understanding the mechanisms behind these effects. Dr. Lipkin thought that the first clue might lie in surveillance. Whereas cancer cells will often go undetected by the

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body's circulating defenses, reversion of the malignant phenotype by CIF led to an increased immune response in both humoral and cellular arms. Increased expression of class I Major Histocompatibility Complex antigens made the tumor cells more susceptible to detection and destruction by cytotoxic T lymphocytes. In melanoma cells CIF also induced the expression of pigmentation antigens that have been shown to enhance antibody-dependent cytotoxicity.


CIF also displays anti-angiogenic activity, interfering with the creation of new blood vessels that may have served a progressing tumor. *In vitro*, CIF almost completely shuts down the ability of melanoma cells to secrete VEGF, a common angiogenic factor. At the same time, CIF inhibits response of blood vessel endothelial cells to another angiogenic factor, bFGF.

Finally, data provided by a chick embryo model suggested that CIF might interfere with metastasis as well.

Biomega Laboratories Inc. was incorporated in 1999 with the expressed purpose of bringing CIF to market for the treatment of cancer. Currently the company has three members on its team - its two scientific founders, Dr. George Lipkin and Dr. Martin Rosenberg (both are faculty at NYU) and Dr. Richard Glaser, the company's chief executive officer. Biomega supports the effort to investigate and develop CIF as a therapeutic candidate through the work carried out in Dr. Lipkin's laboratory as well as collaborations with other groups both within and outside of NYU. One of the most recent and important results of these collaborations has been the isolation and characterization of the single, active constituent of CIF. In addition to seed funding by angel investors, the company has been awarded a NYSTAR grant.

In regard to the future, Drs. Lipkin and Rosenberg believe that given the animal and *in vitro* data collected thus far (Table 1) CIF may be effective against a wide variety of cancers.

Other possible markets for CIF are ophthalmology (diabetic retinopathy, macular degeneration due to aging), dermatology (psoriasis) and the research laboratory. But the first indication will most likely be for malignant melanoma. This disease is the seventh most common cancer in the U.S. and the most common among women ages 25-29. Response rates with currently available therapies are only 20%. The company believes that this makes it an ideal candidate for Fast Track approval by the FDA.

More than 560,000 Americans will die of cancer in 2004. That's nearly twice the number of victims reported in 1966, when Dr. Lipkin began to think about a new therapeutic approach. 

[www.biomegalaboratories.com](http://www.biomegalaboratories.com)

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## CONTACT INHIBITORY FACTOR

**causes the permanent regression of cancers**

**induces the body to destroy cancers through diverse mechanisms**

**halts the growth of cancer cells in culture and restores normal growth controls to these cells**

**reorganizes the cell's actin cytoskeleton**

**makes cancer cells susceptible to detection and destruction by the host's immune system**

**stops the metastasis of cancer cells**

**stops angiogenesis**

**is effective against tumors originating from diverse tissues, including: prostate, breast, colorectal, melanoma, lung, and brain**

**has the potential to be used either alone or in combination with other treatment modalities**

**is non-toxic to the host**