

Pioneering Biochemist Bharat B. Aggarwal, PhD, of the M.D. Anderson Cancer Center, on Discovering Novel and Effective Cancer Treatments

By Karolyn A. Gazella

Bharat B. Aggarwal, PhD, earned his doctorate in biochemistry from the University of California, Berkeley. He completed a postdoctoral fellowship in endocrinology at the University of California Medical Center, San Francisco before working for 10 years with Genetech, Inc., a biotechnology company. While with Genetech, Aggarwal isolated and determined the structure for the first time of two essential components of the immune system that he identified as tumor necrosis factor (TNF)- α and TNF- β . In 1989, Aggarwal accepted the position of professor and chief of the Cytokine Research Section at M.D. Anderson Cancer Center, where he currently holds the Ransom Home, Jr., Endowed Professorship in Cancer Research. He has published more than 500 original articles in peer-reviewed journals.



Q: In 1984, you were part of a group of researchers that identified two novel cytokines. Tell us a little bit about what transpired with your research after you isolated TNF- α and TNF- β .

A: M.D. Anderson was the first cancer center in the country to test our TNF- α in patients with cancer. Although the cytokine was found to be quite active, it was too toxic. Research over the years from our laboratory and others taught us that TNF is the most proinflammatory cytokine and may mediate tumorigenesis and autoimmune diseases. In 1986, David Baltimore discovered a transcription factor, NF- κ B, and went on to report that TNF is the most potent activator of this factor. Because of the critical role of TNF and NF- κ B in tumorigenesis, the focus of our research has been on the discovery of novel inhibitors of TNF and NF- κ B for the prevention and treatment of cancer.

As of today TNF is the key mediator of inflammation, and the annual market for TNF blockers is approaching 20 billion dollars in sales. These drugs are approved for various inflammatory conditions such as rheumatoid arthritis, psoriasis, and inflammatory bowel disease.

Q: Do you feel the connection between inflammation and cancer is widely understood among conventional practitioners and oncologists?

A: I think it is becoming increasingly clear in people's minds. The evidence confirming this connection is accumulating very rapidly. We believe most chronic diseases, including cancer, are caused by inflammation. We have been using conventional and traditional agents as a means for down-regulating inflammation to both prevent and treat a wide array of cancers. The results have been very promising and because of this, the primary focus on my research is in looking at the role of inflammatory pathways in tumorigenesis and other diseases and their modulation by natural products. We have identified several compounds from natural sources, some of which have reached the clinic for the treatment of patients. For example, with the help of clinicians, we have used curcumin for the prevention of lung cancer and for the treatment of multiple myeloma and pancreatic cancer.

Q: What led you specifically to curcumin?

A: As you know I am originally from India, so I naturally have some insight as to what people use there. In India, if you get hurt, have inflammation, break your bone, have a sore throat, or have many other ailments, you take turmeric. Turmeric has been used for centuries. Turmeric contains a component known as curcumin. Curcumin is a significant anti-inflammatory agent in Ayurvedic medicine. It was the historical and traditional use of curcumin that made us want to explore whether it could effectively block anti-inflammatory pathways. We have proven that indeed it does.

Q: You've even completed Phase I and II human clinical trials involving several different types of cancer, correct?

A: We have a number of trials, some have been completed and others are ongoing. It is very exciting and satisfying to have completed clinical trials using curcumin. In addition to curcumin, there are several other anti-inflammatory phytochemicals found in other spices. For example, black pepper, ginger, and clove all have a very similar structure to curcumin. And this is just the tip of the iceberg. There are numerous natural compounds that behave similarly to curcumin. And it appears as though these agents also synergize with each other. Even though we started with curcumin, this is not the only natural agent that is anti-inflammatory; however, we have published many papers specifically on curcumin.

Q: Is it true that there are absorption issues with curcumin and that the dosage needs to be high to produce a therapeutic affect?

A: I think there is a bit of a misconception regarding the absorption and dosage of curcumin. Remember, curcumin is a dietary agent, not a drug. It should not be tested as a drug because if dosages reach the drug level, it could become toxic. We have found that curcumin is circulated quickly and is taken up by tissues very quickly. Within 10 to 20 minutes it is already in the brain. When it is tested as a drug,

researchers are looking for curcumin in serum but they don't find it because it has already been taken up by tissues. In 2008, Marczylo and colleagues demonstrated that very little curcumin was found in plasma and urine in rats after they were given curcumin; however, curcumin was found in intestinal mucosa, as well as liver, kidney, and heart tissue.

Researchers at Johns Hopkins reported that as little as 500 mg of curcumin per day resulted in a 60 percent reduction in polyps, whereas Celebrex at the same dose, which is very cardiotoxic, only resulted in less than 30 percent reduction in polyps as shown by physicians at M.D. Anderson. If bioavailability were an issue, we would not see these results. We have cancer patients at M.D. Anderson who are just on curcumin. They don't have to be given chemotherapy or radiation, just curcumin alone, and we are witnessing significant results. There are more than 1,000 patients on curcumin right now at M.D. Anderson. Absorption of curcumin is not as big of an issue as people may think.

Q: You're not afraid to tackle some of the more challenging cancers. One of your human trials involved pancreatic cancer patients, which is perhaps one of the most deadly and challenging to treat types of cancer.

A: And now researchers in Israel also have done a pancreatic cancer trial, and they have found as many as 50 percent of the patients responded to curcumin. 50 percent is quite impressive in this patient population. That study was presented at the latest American Society of Clinical Oncology meeting. Those same researchers are also now planning multicenter phase III clinical trials.

Q: It can be quite challenging for a cancer patient who wants to use an integrative approach if his/her oncologist is adamant about not using natural substances. Your work is such a deviation from conventional oncology research, what are some of the challenges you've faced?

A: The biggest challenge is for doctors to accept that curcumin could have potential for cancer. Pharmaceutical companies are not going to be able to profit from this. Curcumin is so inexpensive some doctors have a hard time believing that it even works because they are comparing it to drugs that cost \$45,000 to \$50,000 per dose. They feel curcumin cannot work because it doesn't cost as much as the drugs they are used to dispensing. And my response to them is seeing is believing. I tell them to just try it and see if it works.

Q: Why is M.D. Anderson so receptive to what you're doing?

A: I'm in a very fortunate position because the president of M.D. Anderson is a very strong believer. He heard me speak and he saw the evidence and he said, "My god, where have you been hiding?" He could not believe it, and when he talks, everybody else listens. I have a lot of support from him and wherever he goes he talks about the work we are doing with curcumin. Of course, that type of support from the key leadership changes everything. As a result, virtually anyone you talk to at M.D. Anderson knows about curcumin.

There will always be disbelievers. But we are scientists so we just stick to the science and let the results speak for us. People are receptive to options other than chemotherapy and radiation. When you show them that something so economical and safe can also be effective, they become very supportive.

Q: When it comes to your specific research objectives, will you be changing direction or will this remain your focus?

A: My cancer journey that started almost 25 years ago continues with the focus of discovering novel molecules that are safe, efficacious, and yet inexpensive for the treatment of cancer. To do this, we need to move the most promising agents into the clinics to prove that they work for both the prevention and treatment of cancer. We must focus on prevention. The state of Texas has raised 3 billion dollars from taxpayer money and they are going to give 300 million dollars per year for the next 10 years for cancer prevention. That's a lot of money. And it's sending a message about how important prevention must become.

If we continue to prevent and treat cancer the way we are currently doing and have been doing for the past 50 years, the next 50 years will not be any different. We have to learn to think outside the box. We have put too much emphasis on survival of the pharmaceutical companies and not enough focus on the survival of the patients. That's a big problem. We need to change our thinking.

Q: Are we ready for that shift?

A: I think there is a lot of soul-searching going on right now, but I don't think the system is quite ready yet. I think it is becoming even more expensive. That is the case with early diagnosis efforts. Thirty percent of all cancers are indolent cancers. With cancer, in some cases the tiger is sitting there somewhere and needs to be left alone. If you start throwing stones at the tiger, he will strike back. That is exactly what happens with early diagnosis. It is thought that early diagnosis will save lives, but I don't think it does. A good example is prostate cancer. Studies are confirming that early diagnosis of prostate cancer does not save lives. As for breast cancer, researchers have found a 30 percent increase in cancer of women who underwent regular mammograms. In some cases of breast cancer they start treating what they thought was cancer but was not cancer at all. Recent recommendations on early diagnosis of breast cancer screening also suggest that there are more risks involved than benefits. We don't have the foolproof biomarkers of cancer to do early diagnosis properly, so early diagnosis actually ends up doing more harm than good. The biomarkers to detect, prevent and treat cancer are lacking. This makes prevention and treatment very difficult.

About The Interviewer

Karolyn A. Gazella is the coauthor of the *Definitive Guide to Cancer*, *Return to Beautiful Skin* and the newly released *Boost Your Health With Bacteria*. She has been involved in the natural health industry for 18 years. Karolyn is the publisher of the *Natural Medicine Journal* (www.naturalmedicinejournal.com) and has written hundreds of articles on the topic of natural health.

