***Better Questions with Bob Langer***

**Introduction**

**Monologue:** Hey, Max here from GLiMPSE. I got the chance to speak to Bob Langer, and as someone often called the Edison of Medicine he’s full of wisdom:

**Bob:** When you're a grammar school student, high school, college you know you take tests and the way you're judged are grades. And really what those grades reflect is how well you give answers, how well you give answers to other people's questions. But in life really it's not… I mean the answers are important but what's even more important are the questions you ask. You know you could be somebody who spent their whole life asking unimportant questions so they could find the answers to them, but so what? One of the things that I wanted to try to do as a as a mentor is to help guide my postdocs and my students from somebody who's able to give good answers to someone who's able to ask good questions.

**Monologue:** Listen in to learn his story, science, and many more bits of wisdom.

**Some Questions Bob has Asked**

**Bob:** My name’s Bob Langer, and I’m an Institute Professor at MIT

**Monologue:** An Institute Professor is the highest title that an MIT professor can receive, and it’s fitting given Bob’s many accomplishments - winner of the National Medal of Science, inventor on over 1300 patents, and cited an astronomical 283,000 times.

**Bob:** My h-index I think it’s 262, so I think it’s the sixth or seventh highest in the history of the world

**Monologue:** Not surprisingly, Bob attributes his success to the quality of his questions**.** For instance, during his postdoctoral appointment Bob asked two particularly remarkable questions.

First, he asked:

**Bob:** Are there substances that can cause blood vessels to grow or not grow in the body?

**Monologue:** This question propelled Bob to isolate the first angiogenesis inhibitor, a molecule that attenuates the growth of new blood vessels.

 Blood vessel expansion is vital to the growth of tumors. So, a potent angiogenesis inhibitor would be a critical tool in minimizing the severity and spread of cancers.

 But ideally, you’d like the dose of angiogenesis inhibitors given to a patient to only end up in targeted areas where they’re needed - a tumor, for instance.

 And, you’d also like to be able to deliver the drug to this targeted area for an extended period of time - say, a couple of months - as part of a therapeutic regimen.

 These two motivators prompted Bob’s second question:

Bob: Can you come up with plastics that could deliver large molecules for long periods of time?

**Monologue:** This second question drove Bob to deliver isolated angiogenesis inhibitors to tumor cells in the body from a strategically placed polymer encapsulant designed to release the drug at a prescribed rate.

This work is widely cited as a seminal development in modern drug delivery techniques.

**A Look at Bob Langer’s Process**

**Bob:** I guess I've always just tried to judge what I do by impact - will it have a potentially significant impact on the world or not?

**Monologue:** Throughout his career, Bob has consistently asked big questions that have led to significant medical breakthroughs.

But what inspired this habit?

Well, let’s go back to his postdoc days and his first major breakthrough in drug delivery, which we just discussed.

Three contributing factors jump out: drive, perspective and synthesis.

 First, Bob was driven to help because, innately, he likes to help.

**Bob:** When I was a graduate student I helped start a school for poor high school children, the Group School, and there I got very involved in developing new math curricula, new chemistry curricula. And I was very excited about that. I mean Cambridge in the 70s was a very liberal place, and so this school one of the rules was that you didn’t have to take math unless you wanted to.

So, my goal was to see if I could make it exciting and interesting and relevant. And one of things I was very proud of I remember the first year that I taught I think 5 out of 50 people signed up for math and the second year 45 out of 50 did so I felt I was doing something right.

And so that experience I had a really a big effect on me in terms of seeing that I could use my background to help people learn to help people feel better about themselves and things like that.

**Monologue:** Second, his experiences in divergent fields of study gave Bob a unique perspective on medicine in the 1970s.

**Bob:** The one thing that I did maybe a little differently than most people least at the time I did it was I knew something about chemical engineering because it was my major, and then I went to the hospital so I knew something about medicine. And I think a lot of the ideas I’ve had come because I know a little bit about each of those.

**Monologue:** How did this combination of experiences come about? Well, it starts when Bob contemplates his post-PhD future. Like a lot of newly minted PhDs, he didn’t have a clear path ahead of him.

**Bob:** Well what happened was I got my degree here actually PhD or ScD in chemical engineering in 1974 and I think the conventional thing at that time was most of my friends went into the oil petrochemical industry, and I thought about that too. Since everybody else was doing that I thought I should do it so I did a lot of job interviews and I got quite a few jobs at oil companies, but I wasn’t that excited about it. And so, I was trying to look for some way that I might be able to use my chemical engineering background to help people in different ways.

**Bob:** And I ended up well first looking into educational jobs which nobody would hire me for. And secondly to medical jobs which almost nobody would hire me for.

**Monologue:** But then fate intervened with his choice to take a postdoctoral position in a hospital.

**Bob:** But then one person, Judah Folkman, who was a surgeon at Children’s Hospital offered me a job doing medical research and I went there and that was a really a transformative experience for me. I was the only engineer in the hospital and I could see all kinds of medical problems that engineers might think about in different ways.

**Monologue:** Finally, synthesis. Bob was able to synthesize his drive to help, his chemical engineering expertise, and his experiences in the hospital to deliver a new direction for the design of materials used in medicine.

**Bob:** I’ve had this whole sort of central theme of creating much better medical polymers. Before we got involved, almost all polymers that got used in medicine were largely driven by medical doctors. They’d go to their house to find an object that kind of resembled the organ or tissue they wanted to fix. For example, the material in a lady’s girdle - that’s the basis for an artificial heart.

When I saw all this in the hospital I thought well gee rather than take these materials from your house you could come up with strategies for asking the question: “What do you really want in a material from an engineering standpoint, chemistry standpoint, biology standpoint?” and then design them from first principles.

**Monologue:** And Bob’s been able to consistently build from this focus on first-principles engineering throughout his career.

**Bob:** So we have made all kinds of new materials based on that, used them in medicine. They’ve actually led to new treatments for brain cancer and other things. When you create these new materials they can be used for anything.

**Bob’s Future Outlook**

**Bob:** The number of problems that we as a society or as scientists would want to solve or do want to solve, I think they’re enormous. And if you solve some, you know, you raise questions about others, and I really feel they’re never ending.

**Monologue:** So, what are the big medical breakthroughs on the horizon?

What are the big problems to solve, the areas where great questions need to be asked?

**Bob:** Some of the things to me that are really interesting and important are you know new what I’ll call genetic medicines …but how do you then get those genetic medicines to the to the cell to the right part of the body you know to treat the right disease?

There's going to be an enormous future an siRNA, messenger RNA you know gene editing approaches, gene therapy approaches. I think that you know there's so much that can be done there.

I think another big area would be cell therapy…I think that the area is still very young and an awful lot to be done. Could you develop the rules and the scientific understanding for making a new heart, a new pancreas, a new anything?

**Monologue:** Perhaps due to his own journey, Bob has a good sense for the personal characteristics of innovators.

**Bob:** It comes down to a different way of thinking and when you have that different way of thinking, you know, maybe it opens up doors that you never thought of going down but it’ll happen just because of doing something that has a potentially broad impact.

**Monologue:** But, just as experts in medicine of the 1970s did not anticipate the coming revolution in polymer-based drug delivery, Bob cannot predict with confidence what exactly the big innovations of the future will be.

And so, it’s critical to encourage curiosity and serendipity to ensure a productive research agenda:

**Bob:** You want to have some opportunity to do really open-ended, blue sky research whatever it is in whatever area you are. You know, so some of these things that we're talking about, you know, they have labels - like genetic therapies or cell therapies. But my guess is that what you'd almost want to do is do the research that'll create the labels that have never existed before. And what might those be? I mean those would be hard to know because they haven't happened yet.

But by being curious, people will find them. And so, you'd want to have the freedom to do that as well.

**Outro**

**Monologue:** We’ll be back with part two in two weeks.

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Thanks!