

Comment

Everything I need to know about genomics, I learned from Yogi Berra

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"I really didn't say everything I said."

Lawrence Peter (Yogi) Berra

As 2002 draws to a close, I find myself contemplating the future of biology with hope, but also with uncertainty and some apprehension. Will biology continue to be the richest source of discoveries and ideas in all the sciences? Will it become just another Big Science, like nuclear physics, in which the many slave for the enrichment of the few and powerful? Will it bog down in its own arrogance? Will it lose the trust of the public as bioterrorism fears grow and genetically modified organisms try to pervade the marketplace? Or will it become the savior of mankind, ridding the world of disease and famine? And will I be able to get in on any of this?

When I find myself in such a spiritual quandary, I usually turn to a guide - a guru if you will - someone whose wisdom and penetrating insight has served me well in the past. Someone whose wit is equaled only by his clarity of thought. Whose international renown is exceeded only by his stature in the sheltered world of philosophy. I am referring, of course, to Yogi Berra.

Yogi (born Lawrence Peter in 1925 in St. Louis, Missouri) Berra was for many years a baseball catcher (the rough equivalent of wicket-keeper for those of you who play the equally obscure game of cricket) for the New York Yankees, which were, not coincidentally, during his tenure the top team in their sport. Despite his stocky stature he was a great athlete - he was named to the All-Star team fifteen years in a row and three times won the award as the Most Valuable Player in his league - and he was, like his predecessors Sidhartha and Gandhi, a man of simple means and modest needs. He was not given to ostentation or excessive worry about the future - on one occasion his wife, Carmen, asked him: "Yogi, you are from St. Louis, we live in New Jersey, and you played ball in New York. If you die before I do,

where would you like me to have you buried?", and he replied: "Surprise me." Mr Berra displayed in all things the demeanor of the true teacher/philosopher. A man of deep introspection - he is said to have remarked, on seeing a film featuring the late actor Steve McQueen: "He must have made that before he died." - Mr. Berra has given us in his spoken statements (it is not clear whether he can write) a set of observations so clear, so pointedly addressed to the needs of the life sciences today, that we would be fools not to consider them with the reverence they deserve.

True, some Yogi scholars have claimed to find obscurity and bewilderment in these straightforward utterances, but that is doubtless either because they are so used to the deliberate cloudiness of everything in the social sciences and humanities or because they have been laboring under the mistaken assumption that his aphorisms were actually about mundane things such as baseball or life. Once we realize that Yogi, in essentially every comment he has ever offered, is actually talking about biology in the age of genomics, then the mists clear and it becomes apparent that these are the sayings of a sage - perhaps the quintessential sage of our time. As my holiday gift to my readers, I offer this small anthology of just some of his words of wisdom.

"It ain't over 'til it's over"

This is perhaps Mr Berra's most famous aphorism. Although some scholars have speculated that it means a baseball game is not played to any time limit, and therefore the game is not over until the last inning has been completed, clearly a deeper significance is intended here. Yogi is obviously referring to those people who think that genomics is a passing fancy, and that biology will revert to individual-investigator-driven science very soon.

"You can observe a lot by watching"

Mr Berra intends to remind us that computer analysis of reams of data may be fine for the myopic, scientifically

speaking, but there is much to be learned from simply looking at the primary results ourselves.

“When you come to a fork in the road, take it”

Scholars have puzzled over this one for decades (some have been driven mad by it, so such scrutiny is now frowned on), but once one realizes that all of Yogi's dictums refer to genomics the meaning becomes clear. Biology is at a fork in the road - it can either go down the path of big science or try to maintain its 'small is beautiful' character as much as possible. Mr. Berra's preference is obvious.

“Nobody goes there anymore, it's too crowded”

In a profound comment on the herd mentality so prevalent in biology today, Yogi is reminding us that the road less traveled often contains the most interesting possibilities. He warns us that creative minds eschew the crowd.

“This is like *deja vu* all over again”

By this Yogi clearly means that the current fad for all things genomic (for example, cDNA microarray analysis of everything under the sun) is in many respects a recapitulation of earlier fads for site-directed mutagenesis, protein structure determination by X-ray crystallography, signal transduction, and so on. All these 'new sciences' eventually became more-or-less routine laboratory techniques. It can happen to any new discipline, and it probably always will.

“In theory there is no difference between theory and practice. In practice there is.”

Can one imagine a more important observation in the age of genomics? As we rush to draw conclusions - general ones, at that - from genome sequences and microarrays and protein structure databases, Yogi reminds us that there is no substitute for careful experimentation. Because Nature has a nasty habit of surprising us just when we think we have Her figured out.

“A nickel ain't worth a dime anymore”

Mr Berra is obviously commenting on the enormous cost of genome-driven biology, and urges the funding agencies to increase the average award size immediately. His words are directly addressed to the program officer who administers my grants.

“The future ain't what it used to be”

To which one can only say: How true.

“You've got to be very careful if you don't know where you are going because you might not get there,” and “If you don't know where you are going, you might wind up someplace else”

Phil Rizzuto (a teammate) said “Hey Yogi I think we're lost.” Yogi Berra replied “Ya, but we're making great time!” Clearly this is a recurring theme in Mr Berra's work: the journey; the voyage through life that we all undertake. He wishes us to

understand that biology, too, is on a journey, and its ultimate destination - or even the route it is following - is unclear. As scientists we tend to shun planning for the future of our discipline, preferring to go with flow, so to speak, and be carried along towards whatever shore the current is tending. In this cluster of sayings, we see that such insouciance sometimes has a price - namely shipwreck. Yogi would have us sometimes pause, and consider where we would like to end up, and adjust our course accordingly.

“It was impossible to get a conversation going, everybody was talking too much”

This is the one saying of Yogi's that does not explicitly refer to genomics. I believe he is commenting here on academic committee meetings, but some scholars differ in interpretation.

“There are some people who, if they don't already know, you can't tell 'em”

And most of them, for some reason, now seem to work in the general area of analysis of large genomics-driven databases.

“If you can't imitate him, don't copy him”

What words to live by. Yogi reminds us here that copying is easy, but to be as good as the person imitated is not. As we all scramble to reinvent ourselves, and retool our experiments and our ways of thinking to match those of the genomicists who are receiving so much publicity and funding these days, it is well to keep in mind that sometimes we do best by just being ourselves. As Mr Berra might have said (but didn't - although with him one can never be sure): You are what you are.

“You should always go to other people's funerals; otherwise, they won't come to yours”

I don't have the slightest idea what Yogi really meant by this statement. And I'm willing to bet that he doesn't either.

Editor's note: interested readers can learn more about Yogi Berra at his official website, <http://www.yogi-berra.com/>