Want new medicines? You need fundamental research

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Would we be wise to prioritize "shovel-ready" science over curiosity-driven, fundamental research programs? Would that set the stage for the discovery of more new medicines over the long term?

To find solid answers to these questions, scientists at Harvard and the Novartis Institute for Biomedical Research (NIBR), publishing in *Science Translational Medicine*, looked deep into the past discovery of new drugs and showed that, in fact, fundamental research is "the best route to the generation of powerful new medicines".

"The discoveries that lead to the creation of a new medicine do not usually originate in an experiment that sets out to make a drug. Rather, they have their origins in a study—or many studies—that seek to understand a biological or chemical process," explains Mark Fishman, one of three authors of the study. "And often many years pass, and much scientific evidence accumulates, before someone realizes that maybe this work holds relevance to a medical therapy. Only in hindsight does it seem obvious."

Fishman is a Harvard Professor of Stem Cell and Regenerative Biology, a faculty member of the Harvard Stem Cell Institute, and former President of NIBR. He is a consultant for Novartis and MPM Capital, and is on the board of directors of Semma Therapeutics and the Scientific Advisory Board of Tenaya Therapeutics.

Utility Seen in Hindsight

CRISPR-cas9 is a good example of discovery biology opening up new opportunities in therapeutics. It started as a study of how bacteria resist infection by viruses. Scientists figured out how the tools that bacteria use to cut the DNA of an invading virus could be used to edit the human genome, and possibly to target genetic diseases directly. The origins of CRISPR-Cas9 were entirely non-utilitarian, but those discoveries have the potential to open a whole new field of genomic medicine.

Yet some believe that projects that can demonstrate, up front, that they could produce something useful should take priority over projects that

explore fundamental questions. Would we have many more medicines if academics focused more on programs with practical outcomes? How would that shift affect us in the future?

The Study

To find answers, Fishman and his colleagues investigated the many scientific and historical paths that have led to new drugs. The study they produced is a contemporary look at the evidence linking basic research to new medicines.

The authors used a list of the 28 drugs defined by other scientists as the "most transformative" medicines in the US between 1985 and 2009. They determined whether the drug's discovery began with an observation about the roots of disease, whether the biologist believed that it would be relevant to making a new medicine, and how long it took to realize that relevance. To mitigate bias, they repeatedly corroborated the assignment with the outside experts.

What They Found

Eight out of ten of the medicines on the list led back to a fundamental discovery—or series of discoveries—without a clear path to new drug.

The average time from discovery to new drug approval: 30 years, the majority of which is likely to have been in academia, before pharmaceutical or biotechnology companies started the relevant drug development programs.

"We cannot predict which fundamental discovery will lead to a new drug," Fishman concludes. "But I would say, from this work, and my experiences both as a drug discoverer and a fundamental scientist, that

the foundation for the next wave of great drugs is being set today by scientists driven by curiosity about the workings of nature."

More information: J.M. Spector el al., "Fundamental science behind today's important medicines," *Science Translational Medicine* (2018). stm.sciencemag.org/lookup/doi/ … scitranslmed.aaq1787

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