The right drugs for the job : the use of antimetabolites in biological research (1940-1960)

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Abstract

With the advent of the sulfa drugs in the mid-1930s came the so-called era of the wonder drugs, which raised considerable hopes that medicine could be revolutionized through the power of chemotherapy. In 1940, a young biochemist, Donald D. Woods, presented consistent proofs that sulfa drugs acted by interfering with an essential metabolite, a substance necessary for cell growth. This was the main starting point for the expansion of the theory of antimetabolites, which was rapidly thought of as providing a general mode of drug discovery. As such, it generated a lot of disillusion, although it also produced some lasting therapeutic successes.
In the meantime, the fields of biological and medical research were being "molecularized" through the understanding, visualization and manipulation of mechanisms situated within the cell. Some of the newly synthesized antimetabolites were used as biological research tools, to unravel metabolic pathways, identify essential metabolites, understand the biochemistry of nucleic acids, and produce detailed knowledge concerning the functioning of enzymes.
This paper analyses the interplay between research in fundamental biology and drug discovery exemplified by the antimetabolites. Thus, this case study seeks to connect the history of drugs and pharmacology with the history of biochemistry and molecular biology.

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