molecular parameters of interaction partners *in vitro* or on a cellular level. Then, the biochemists' dream of understanding the physiology of life on a molecular level might meet with the drug discoverers' dream of understanding the biochemical mode-of-action of a compound already after the primary screening phase.

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Phage display: increasing the rewards from genomic information ▼

These are interesting times in the ongoing war between humans and bacterial pathogens. Until recently, it appeared that the development of penicillin and other antibiotics had guaranteed victory but, unfortunately, it has become clear that the excessive use of these same antibiotics has led to the evolution of resistant bacterial strains that threaten to overwhelm human health. Thus, we again find ourselves in desperate need of new weapons against bacterial pathogens.

While bacteria have been busy evolving new forms of resistance, humans have been busy unraveling genomes. Whole-genome sequencing has provided access to the complete proteomes of dozens of bacterial species and, in doing so, has revealed numerous potential targets for antimicrobial action. In a recent review in *Drug Discovery Today*, Christensen *et al.*[1] point out that any essential protein could be a target for antibacterial drug discovery but, to effectively use this genomic information in drug development, two important goals must be achieved. First, newly discovered proteins must be validated as legitimate targets for therapeutic intervention and, second, high-throughput screens must be developed to enable rapid identification of compounds that inhibit protein function. Christensen and coauthors convincingly argue that phage-displayed combinatorial peptide libraries can aid both these goals.

Using current optimized methods, phage-displayed peptide libraries containing tens of billions of different sequences can be readily constructed and used to select specific ligands against essentially any protein of interest[2]. Thus, highly specific peptidic-ligands can be obtained rapidly without any previous knowledge of a protein's function. These ligands can then be used for target validation and HTS. For example, binding peptides can be expressed inside a bacterial cell and, in such a system, growth inhibition can be used as strong evidence that the peptide's binding partner is an essential protein, and thus, a potential drug target[3]. The same peptides can then be used to set up high-throughput assays to identify small molecules that bind at the same site and inhibit protein function[4]. In this way, new targets and inhibitors could quickly be obtained with only a minimal knowledge of a protein's structure and function.

The approaches described by Christensen and coauthors are indicative of a larger trend in the life sciences. The full benefit of genomic information can only be realized with combinatorial approaches that speed up the process of characterizing the tens of thousands of proteins that comprise a living proteome. Phage display and other combinatorial biology methods have a major role in modern biological research[5], and this role will continue to expand as we tackle the difficult, but highly rewarding, task of deriving novel therapeutics from genomic information.

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