Preface

Clustered regularly interspaced short palindromic repeats (CRISPR), together with associated sequences (*cas* genes and Cas proteins) form the CRISPR-Cas adaptive immune system, which is present in most archaea and many bacteria. This relatively novel family of repeats was first discovered in 1987, characterized in 2002, implicated in immunity in 2005, and shown to provide acquired resistance against bacterial viruses in 2007. Since, it has been implicated in providing adaptive immunity against bacteriophages, archaeal viruses, and plasmids in numerous organisms. The development of several functional model systems in the recent past has paved the way for thorough scientific investigations of these unique and intriguing defense systems.

Notwithstanding extensive sequence diversity and gene content polymorphism, CRISPR-Cas systems have recently been categorized into three types, based on phylogeny and molecular mechanism of action. This has set the stage for a revision of the nomenclature, and collective agreement on terminology, representation standards, and definition of the various stages that render CRISPR-mediated immunity. Mechanistically, CRISPR-Cas systems drive immunity through three major steps: (1) *acquisition*, where immunization occurs by uptake of foreign DNA sequence and integration as new CRISPR spacers; (2) *expression*, where Cas proteins are produced and CRISPR-encoded transcripts are processed into small interfering CRISPR RNAs (crRNAs); (3) *interference*, where crRNA-Cas ribonucleoprotein complexes mediate homologous target recognition and specific cleavage. The ability of this idiosyncratic system to integrate short DNA sequences from invasive elements into the chromosome renders adaptive immunity inheritable.

This book provides a unique perspective into the historical events and key discoveries that have unraveled the functions of CRISPR-Cas systems and the roles they play in bacterial and archaeal biology and evolution. Once the occurrence, diversity, function, and evolution of CRISPR are established, each CRISPR-Cas type is specifically characterized. Their roles in various biological processes (not restricted to defense) are discussed, and applications are outlined. Their impact on microbial populations and evolutions are outlined, thus setting the stage for a deeper understanding of CRISPR-Cas systems.

Although there are mechanistic commonalities between CRISPR-mediated immunity and RNAi, notably small non-coding RNA-mediated cleavage of complementary target nucleic acid sequences (generally DNA, but one sub-type eliminates RNA) by a ribonucleoprotein complex, there are fundamental differences in the molecular processes that drive these two phenomena. Functionally, in addition to providing adaptive immunity against exogenous viral and plasmid dsDNA, at least some CRISPR-Cas systems appear to play a role in host-regulatory processes. Several applications have been established, notably build up of phage resistance, and exploiting hypervariability for typing and epidemiological surveys. Moreover, the ability to re-program the cleavage machinery has opened new avenues for customized DNA restriction, nicking, genome engineering and editing.

Some of the contributors have been intimated with CRISPR sequences for many years, and provided their personal perspective on this fast-evolving and exciting field. Likewise, several authors have been very active members of the CRISPR research community and have had the privilege to participate in the annual CRISPR meetings hosted at UC Berkeley since 2008, and at Wageningen University in 2010. The material presented here illustrates the frenetic pace at which the field has evolved over the last five years, and the breadth and scope of topics discussed reflect the scientifically diverse community which has come together, covering foci including molecular studies, genetic analyses, mathematical modeling, evolution, functional implementation, epidemiology, metagenomics, and ecology. The variety of entry ways into the field, and diversity of the vantage points of the various groups involved illustrates the relevance of the topic. Current implementation of CRISPR-Cas systems to develop phage resistance in dairy starter cultures has already shown that CRISPR can be leveraged industrially. Current analyses of CRISPR polymorphism in pathogenic species will determine how relevant these loci may be for epidemiological surveys, clinical analyses, and food safety.

We would like to acknowledge all the authors, our colleagues, collaborators, and CRISPR meeting participants for all their contributions to the field, colorful opinions, and insightful conversations.

Looking back, the significant advances in studying the CRISPR mechanism of action have set the stage for applications and areas of investigation, and establish a solid basis for future studies that will investigate the outstanding mysteries and questions that remain unanswered. We are hopeful that the need for proper bioinformatics tools will be addressed, and that NCBI will integrate CRISPR-related resources. Doubtless, we predict that the community camaraderie and scientific diversity will pave the way for a bright future of CRISPR as a field. Certainly, the visibility of the field as measured by ever-increasing quantity, spectacular quality, and impressive citation rates of CRISPR-related publications warrant a bright future. This may just be the beginning…

http://www.springer.com/978-3-642-34656-9

CRISPR-Cas Systems
RNA-mediated Adaptive Immunity in Bacteria and Archaea
Barrangou, R.; van der Oost, J. (Eds.)
2013, X, 302 p., Hardcover
ISBN: 978-3-642-34656-9