Data accumulated by human genome sequencing will allow healthcare providers to customize treatments for patients with precision medicine and conduct genetic testing to confirm diagnostics. Sequencing the genomes of pathogens will also enable researchers to gain new knowledge about the mechanisms of disease, and may lead to the creation of better therapeutics (Norquist and Swisher 2015, Ostrov et al. 2019).

Massive amounts of sequencing data have permitted increased understanding of the molecular determinants of pathogenesis, that is, the manner of development of a disease. During outbreaks, the ability to sequence multiple genomes of pathogens with rapidity and precision has helped researchers to track transmission and the emergence of outbreaks, to assist with contact tracing, and to determine how specific mutations accumulated during an outbreak might have contributed to the speed of transmission (Wohl, Schaffner, and Sabeti 2016). Sequencing has been used during the COVID-19 pandemic to track the spread of SARS-CoV-2 from country to country and to better understand both transmission chains and the interaction between the virus and animal hosts (Bugembe et al. 2020; Goes de Jesus 2020; Meredith et al. 2020, Zhang and Holmes 2020).

The process of DNA sequencing is continually evolving. Current widespread methods that were developed in the 2010s under the heading 'third generation sequencing' relied on the convergence of microfabrication, high-resolution imaging and advances in computational power (Giani et al. 2020). Single molecules of DNA were directly sequenced without an amplification step. Over time, this approach led to longer segments being analysed in a single run. This development is important as longer segments are more easily assembled by overlapping sequences, and since 2010 larger and larger genomes have been sequenced in their entirety with great rapidity. In addition, nanopore-based technologies enable entire genomes to be read in a non-destructive manner, thus enabling sample conservation, unlike traditional methods that segment the genome (Kono and Arakawa 2019).

Single cell RNA sequencing technology has also been useful for more subtle analyses, such as identifying cell subpopulations or regulatory network components by examining the specific RNAs synthesized in individual cells. The next stage in sequencing technology is 'fourth generation sequencing', also called *in situ* sequencing or massively parallel spatially resolved sequencing. This combines advanced microimaging and next generation sequencing to define tissue heterogeneity. Fourth generation sequencing is useful in diagnostics and basic research to understand how cells control expression of their genes (Ke et al. 2016).

Security Implications of DNA Sequencing

Progress in the area of DNA sequencing has generated considerable benefits, such as rapid diagnosis of disease or analysis of samples of high complexity, leading to maturation of fields such as microbial forensics and personalized medicine. However, this information could also be exploited for the generation of powerful new strains of viruses, with increased transmissibility and virulence (National Academies 2015). In the area of human genetics, there is great concern that exploitation of population sequence analysis could even conceivably lead to the malicious targeting of specific populations or individuals with biological weapons (Khoury, Iademarco, and Riley 2016).

Gene and genome modification

Vast improvements in sequencing technologies have been accompanied by more precise tools and methods to modify genes. While genome modification has been practiced for decades, 2013 ushered in a remarkable new approach: Clustered Regularly Interspaced Short Palindromic Repeats, or CRISPR (Hsu, Lander, and Zhang 2014; Jinek et al. 2012). This methodology allows the simple and precise alteration of specific gene sequences through the use of a combination of RNA and proteins. The "guide" RNA directs the DNA-

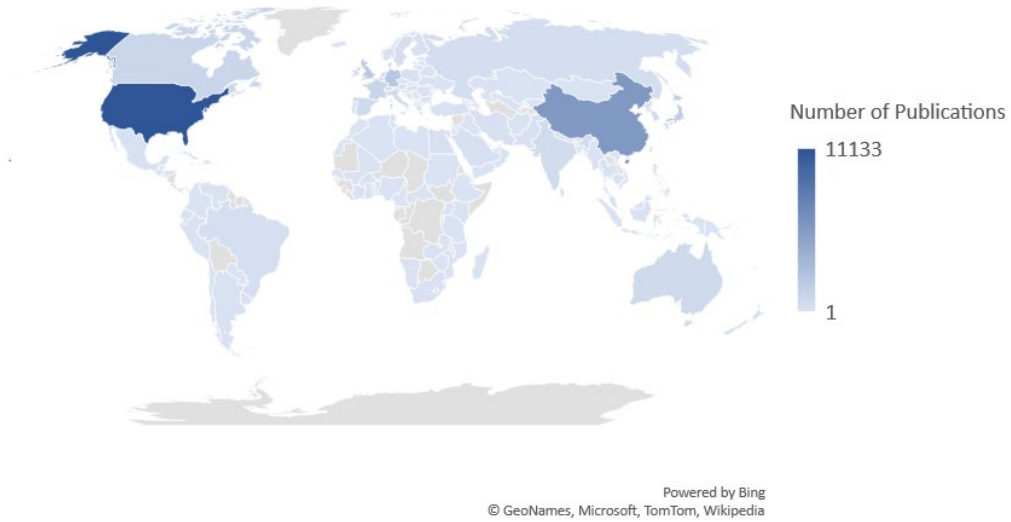

Figure 2. ***Map showing the intensity of scholarly publications referring to CRISPR by country.***[3]

editing proteins to a precise location in a chromosome, where they proceed to delete and/or replace the target site with new DNA sequences. The method was quickly commercialized—within months of the first publications—and is now universally available and applicable to any genome within any kind of cell, whether bacterial, animal or plant. Scientist around the globe are now exploring CRISPR technology, something illustrated in Figure 2 above, which shows the extent of scholarly publications discussing CRISPR.

CRISPR and other gene editing methods have the potential to revolutionize medicine by making it possible for scientists to target specific genes with highly specific modifications (Dominguez, Lim, and Qi 2016). Already, CRISPR has been used for general research purposes allowing rapid and precise alteration of genes in multiple experimental systems. Targeting and editing human genes opens-up the possibility of eliminating certain genetic diseases in individuals (Anzalone et al. 2019; Dunbar et al. 2018; Li et al. 2019). For example, CRISPR gene editing has been used in humans to treat sickle cell disease (Bourzac. K. 2017).

Security implications of gene and genome modification

New gene editing tools can be used to alter plants, animals, and insects, as well as somatic (non-inherited) and germline (inherited) or embryonic cells, including in humans. CRISPR is also used in the development of novel detection, diagnostic and therapeutic tools (Abbott et al. 2020). Moreover, in the burgeoning global bioeconomy, genetically modified organisms have been created to produce high-value compounds, such as therapeutic drugs, in a more flexible and sustainable manner (National Academies 2020). As such, gene and genome modification have positive implications for security.

However, the technology has also raised security concerns (Clapper 2016). Scholars have discussed the rapid advances, ease, and availability of CRISPR in genetic editing technologies as aiding the development of biological weapons by both State and non-State actors. It has been argued that States and non-State actors with limited resources would find the low cost and relatively easy access attractive for the development

3 This map has been produced by the authors using the search term "TITLE-ABS-KEY (crispr)" in the publication database SCOPUS. Of the 26,630 publications with CRISPR in the title, abstract or keywords, 1420 were of an undefined origin.