**Worksheet 2 Finding a treatment**

Learning Objective: This worksheet introduces students to some of the approaches for treating and managing the COVID-19 pandemic.

An interview with the founder of SynBioBeta John Cumbers by [RT America](https://www.youtube.com/watch?v=eLu1YSjGV-M&feature=youtu.be) discusses the efforts of scientists and doctors to develop a treatment for COVID-19. The brief video introduces the concept of synthetic biology and some of the early efforts in developing potential treatments against SARS-CoV-2 infection. In the video, different approaches to developing a treatment are discussed. These approaches include repurposing previously approved drugs, use of purified antibodies from recovered patients (passive immunity), and the development of vaccines (Figure 1). These approaches are both short-term and long-term in dealing with COVID-19 and any other viral diseases that we may experience in the future.

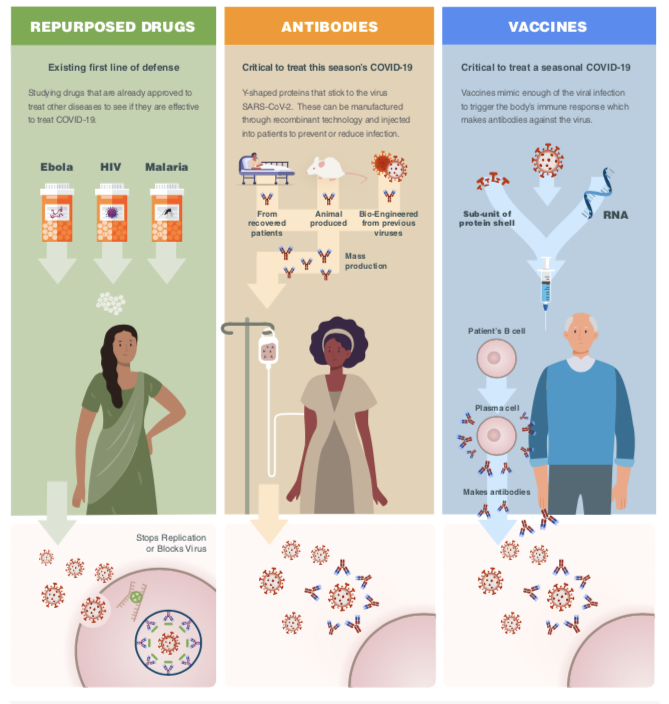


Figure 1. Varied approaches to treat COVID-19. (Image used with permission from SynBioBeta (http://[www.synbiobeta.com/COVID19](http://www.synbiobeta.com/COVID19))).

The viral infection cycle involves the binding of the virus (attachment) to specific cell types through the interaction of one or more viral coat proteins and one or more eukaryotic cellular transmembrane proteins. Once attachment has occurred, the viral particle (virion) delivers the genome (RNA in the case of SARS-CoV-2) into the cell. This genome is replicated (RNA dependent RNA polymerase) and viral proteins are synthesized by the host cell. The new virion is then packaged to be released from the cell.

Repurposed drugs - The idea is to use drugs that have previously been approved by the Federal Drug Administration (FDA) for the treatment of a specific disease to be used as a treatment of individuals with COVID-19 infections. The FDA approval process is long and commonly entails three phases of clinical trials before it is licensed for use . The phase I tests safety of the drug, phase II looks at the efficacy of the drug in treating the disease or condition, and phase III confirms efficacy in large populations and monitors side effects. The repurposed drugs have the advantage that they have been deemed safe in regards to the FDA standards, which allows the drugs to be used in Phase II trials earlier to test efficacy (effectiveness) (Figure 2). While these drugs have been approved to be used for a variety of infectious agents, their effect on the SARS-CoV-2 virus is currently untested.



Figure 2. Schematic of Federal Drug Administration drug approval process. (Image used with permission from SynBioBeta <http://www.synbiobeta.org/COVID19>)).

The listing of repurposed drugs shown in Table 1 was obtained from [COVID-19 Treatment and Vaccine Tracker](https://milkeninstitute.org/sites/default/files/2020-03/Covid19%20Tracker%20032020v3-posting.pdf). To find the approved purpose and function, go to [DrugBank](https://www.drugbank.ca/) and look up the specific drug listed in the first column. Then fill out the next two columns based on the information you gathered.

Table 1. Some of the repurposed drugs that are being investigated for treatment of COVID-19.

|  |  |  |
| --- | --- | --- |
| **Repurposed drug** | **Approved purpose** | **Function** |
| Remdesivir |  |  |
| Lopinavir |  |  |
| Hydroxychloroquine |  |  |
| Baloxavir marboxil |  |  |

Antibodies - Upon infection, an individual mounts an immune response against parts of the virus (or other invading organism). As part of the adaptive and specific immune response to the virus, the individual’s B cells produce antibodies that can specifically bind to some part of the introduced virus, cell or protein (Figure 3). Individuals who have recovered from the COVID-19, are likely to have developed specific antibodies against the SARS-CoV-2 virus. These antibodies can be purified from their blood plasma and then infused into another patient as an immediate short-term passive immunity against the infectious agent. This is a century-old practice and commonly sometimes used during large-scale epidemics. This is particularly important since developing a vaccine and mounting an immune response takes some time (Figure 3).

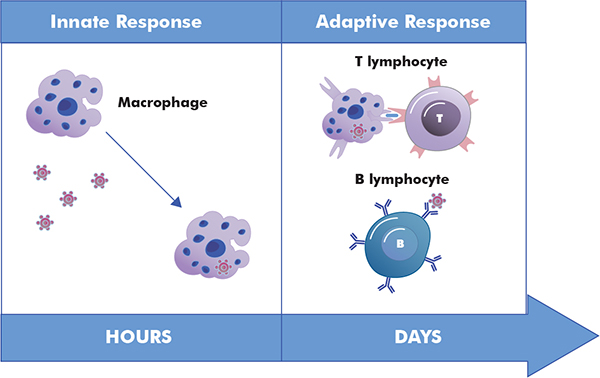


Figure 3. Mounting an immune response against a specific antigen takes some time. (Image used with permission from © 2020 Novus Biologicals™ a Bio-Techne® Company

<https://www.novusbio.com/research-areas/immunology>).

Vaccines - Vaccines are generated by introducing a viral protein or an attenuated (viable but weakened) virus or inactivated virus into an individual so that they can develop immunity against the infecting agent. Administering vaccinations to children at an early age has been used successfully to protect people against a wide variety of viruses and bacteria that have caused severe human disease in the past (Table 2). Please watch the brief video on the purpose of [childhood vaccinations](https://vimeo.com/217903624).

Table 2. Select CDC Childhood vaccination schedule (<https://www.uspharmacist.com/article/childhood-vaccinations>)

|  |  |
| --- | --- |
| **Vaccine** | **Ages (number of doses)** |
| Hepatitis B | Birth-18 months (3) |
| Diphtheria, tetanus and pertussis (DTaP) | 2-18 months (4); 4-6 years (1) |
| *Haemophilus influenza* type b | 2-5 months (3 or 4) |
| Pneumococcal conjugate | 2-15 months (4) |
| Inactivated poliovirus | 2-18 months (3); 4-6 years (1) |
| Influenza | annual , 6 months |
| Measles, mumps, rubella | 12-15 months (1); 4-6 years (1) |
| Meningococcal | 11-12 years (1); 16 years (1) |
| Human papillomavirus | 11-12 years (1) |

One new approach to vaccination is the use of a specific mRNA molecule instead of a protein or virus as the agent introduced into a patient. One of the first vaccination trials using this new approach to elicit immunization against COVID-19 started even before the major outbreak of COVID-19 in the United States. The company [Moderna](https://www.modernatx.com/) began producing an mRNA drug that encodes the viral SARS-CoV-2 Spike (S) glycoprotein. The delivery of the drug, through lipid vesicles to lymph nodes, allows the patient cells to produce the Spike protein on the surface of the cell and develop immunity. For an overview of this process, watch this [Moderna video](https://www.youtube.com/watch?time_continue=54&v=qJlP91xjvsQ&feature=emb_logo).

**Questions:**

1. What are some advantages and disadvantages of using repurposed drugs, antibodies and vaccines in an outbreak?
2. What are some of the cellular or viral targets for the repurposed drugs (see your completed Table 1)? Why might someone choose to test one of these drugs?
3. How do you think scientists and doctors determined which repurposed drugs might be effective in testing against SARS-CoV-2? *Think about the purpose that the drugs serve in treating the approved disease from Table 1.*
4. Why is it recommended that you receive a seasonal influenza vaccination each year?
5. How might the approach by Moderna (injecting mRNA) speed up the process of vaccination? How will the B-cell use the mRNA to produce and present the Spike protein?