

Table 5  
 COVID-19 Current Vaccine Development Techniques. Adapted from [145]

COVID-19 Vaccines Techniques							
Attenuation	Inactivation	Fractionation		Cloning		Expression	
Codagenix/ SII	SinoVac/ Dynavax	Non-recombinant purified purified subunit		Cloning		Protein	
				<b>Replication competent virus vector vaccine</b>	<b>DNA Vaccine</b>		
		Clover Bio- pharm/GSK	Novavax	Tonix Pharma/Southern Research	Inovio/Beijing	Virus-Like Particle vaccine	Subunit Vaccine
		Baylor/UTMB/ NYBC/Fudan	Vaxart	Altimune	Advaccine	Geovax labs/Bravovax	Clover Biopharm/ GSK
		UQ/GSK/ Dynavax	Generex	Greffex	Biotech	Medicago	Baylor/UTMB/ NYBC/Fudan
		Generex/ EpiVax	ExpreS2ion	Vaxart	Applied DNA Sciences		UQ/GSK/ Dynavax
		Sanofi Pasteur	Vaxil Bio	Zydus	Takis Biotech/Evvivax		Generex/ EpiVax
		Walter Reed/ USAMRIID	EpiVax/ Ugeorgia	Cadla	Zydus Cadila		Sanofi Pasteur
		iBio/CC- Pharming		Institute Pasteur			Walter Reed/ USAMRIID iBio/CC- Pharming
				<b>Non- replicating viral vectors</b>	<b>RNA Vaccine</b>		
				CanSino (Ad5)	Moderna/NIAID		Novavax
				J&J/BARDA (Ad26)	CureVac		Vaxart
				Unjv. Oxford (ChAdOx1)	Arcturus/Duke/NUS		Generex
					BioNTech/Pfizer		ExpreS2ion Vaxil Bio EpiVax/ Ugeorgia

The laboratory findings showed an increase in peripheral lymphocytes, a decrease in CRP, the complete resolution of the overactivated cytokine secreting immune cells like CD4+ T-cells, CD8+ T-cells, and NK cells, a reduction in TNF- $\alpha$ , and an increase in IL-10.

The intravenous infusion of MSCs looks to be a safe alternative for treating patients with severe cases of COVID-19. Despite this data, further studies in a more significant population cohort are needed to corroborate this therapeutic intervention [151].

A study demonstrated the presence of S- reactive CD4+ T cells in COVID-19 patients and also in unexposed healthy individuals. These pre-existing S-reactive T-cells could be cross-reactive clones obtained in prior infections with endemic HCoV that account for ~20% of the yearly common cold.

The function of the pre-existing S-cross-reactive CD4+ T-cells in 35% of the healthy individuals is

still unknown; however, if these cells are protective in a SARS-CoV-2 infection, they could provide some understanding in the different manifestations of COVID-19, and shed some light in why children and young adults appear to be more resistant to symptomatic SARS-CoV-2 infection [152].

#### *Allogeneic cardiosphere-derived cells*

In a series of non-randomized cases of 6 COVID-19 positive patients, with an age range of 19–75 years, cardiosphere-derived cells (CDCs) were used to treat patients who were positive for and exhibited lung injury. CDC's mechanism of action is to target several cytokine pathways (e.g., IL-1, IL-6, TNF $\alpha$ ), which levels decreased after the infusion. All patients showed clinical recovery and were extubated [153].