

Objective: To investigate the possibility of adverse neurological events associated with administration of COVID-19 vaccine in rodents and healthy human volunteers.

Abstract:

On 16th January 2021, India launched a massive COVID-19 vaccination drive using two vaccines: Covishield, a weakened adenoviral vector carrying the gene for SARS-CoV-2 spike protein, and the second vaccine Covaxin, an inactivated coronavirus. Inactivated viruses have been used as vaccines for diseases such as rabies, hepatitis A and polio for several decades. The adenoviral platform has not been used in an approved vaccine, although it has been tested in experimental vaccines against other viruses such as the Ebola virus. Adverse events associated with vaccinations have always been a source of much concern, and therefore it is essential to obtain evidence of the safety of a vaccine through animal studies as well as from healthy human volunteers. In this project, we will address the possibility of adverse neurological events associated with administration of the adenoviral as well as inactivated coronavirus vaccines in India.

Methodology:

This study will be divided into two phases:

Phase 1: The vaccine will be administered to healthy rodents, and monitored over a period of 8 weeks-12 weeks. The animals will be sacrificed at various time points during this period to investigate inflammation and histological abnormalities in tissues obtained from the CNS and PNS. Brain tissue edema, neuronal degeneration, presence of demyelinating lesions or inflammation in brain and spinal cord, and antibody levels in serum and cerebrospinal fluid will be assessed.

Phase 2: Healthy human volunteers will be monitored for neurological symptoms, which will further be divided into three categories:

- ✓ CNS symptoms (headache, dizziness, impaired consciousness, ataxia, acute cerebrovascular disease, and epilepsy).
- ✓ PNS symptoms (hypogeusia, hyposmia, hypopsia, and neuralgia).
- ✓ Skeletal muscular symptoms.

The human volunteers will include those who have been inoculated with either of the two vaccines, as well as those who have not been vaccinated. We are in the process of discussion with SVIMS. We have institutional ethical committee and Institutional Biosafety committee and we will process to apply for approvals.

Budget:

S.No.	Head	Total (INR)
1.	Manpower	1,80,000
2.	Consumables	8,00,000
3.	Equipment	6,00,000

4.	Transportation costs	60,000
5.	Animal maintenance	1,00,000
5.	Contingencies	30,000
6.	Other costs	30,000
7.	Institute Overhead	3,00,000
8.	GRAND TOTAL	30,00,000

Justification: One Research Assistant will be hired for the entire duration of the project, and will plan and conduct experiments for Phase 1 and 2 along with the PI. Equipment money will be utilized to purchase a high-precision semi-automated microtome for accurate sectioning of CNS tissue samples for histological experiments, which will be crucial in this project. Animals will be purchased and maintained at the SV University in Tirupati for a duration of 10 weeks. Transportation costs will be used to transport both types of vaccines at 4°C and to transport the mice to the animal facility at Tirupati. Consumables money will be utilized to purchase antibodies, enzymes and reagents for histology studies, markers for inflammation and neuronal degeneration, ELISA assay kits for detecting antibody levels, plastic ware, glassware and other aiding consumables. Contingencies and other costs comprise costs towards printing material, scanning, paper and other unexpected expenditure that may be incurred throughout the duration of the project such as equipment maintenance, petty expenditures etc.

Timeline:

Activity		Time in Months					
		1	2	3	4	5	6
		Administrative Work					
Hiring Research Staff							
Procurement of vaccines, Installation of equipment, and Training for use							
		Proposed Research Work					
Phase 1	Purchase and acclimatization of rats at the animal facility at SV University.						
	Administration of Covishield or Covaxin vaccines to rats.						
	Sacrifice rats every 2 weeks. Process, fix and store tissues, CSF, serum for histology and cell biology experiments.						
	Histology and biochemical assays to detect neurological aberrations, lesions, inflammation.						

Phase 2	Collaboration with SVIMS hospital, Tirupati to monitor neurological symptoms in vaccinated human volunteers.						
	Neuroimaging using MRI to validate findings in humans.						
	Preparation of manuscripts and closure of project.						

 In collaboration with SVIMS hospital, Tirupati.