

COVID-19 through Adverse Outcome Pathways: Building Networks to Better Understand the Disease – 3rd CIAO AOP Design Workshop

Supplementary Data

Annex A: Key events

Wiki KE ID	CIAO KE ID	KE title	biological organization	KE position	WG (1 st round)	WG (2 nd round)
188	23	Neuroinflammation	3. tissue	4. late	orange, red	
351	72	Mortality	5. individual	5. AO	?	
352	37	Neurodegeneration	3. tissue	4. late	red	
709	69	Cell death, kidney cells	2. cellular	3. middle	yellow, red	
814	70	Kidney injury	4. organ	5. AO	red	other organs
902	66	Inflammation, liver	3. tissue	3. middle	orange, red	
952	61	Blood pressure, increase	3. tissue/organ	4. late	red	
1043	54	Hypertrophy (heart)	3. tissue	4. late	red	
1375	45	Platelet aggregation	1. molecular	3. middle	yellow, orange, red	Hub
1392	16	Oxidative stress	2. cellular	3. middle	orange	Hub
1458	53	Lung fibrosis	4. organ	5. AO	red	Lung
1492	18	Tissue resident cell activation	2. cellular	3. middle	orange	Hub
1493	19	Increased pro-inflammatory mediators	2. cellular	3. middle	orange	Hub
1494	20	Leukocyte recruitment / Activation	2. cellular	3. middle	orange	Hub
1496	19	Increased pro-inflammatory mediators	2. cellular	3. middle	orange	Hub
1497	20	Leukocyte recruitment / Activation	2. cellular	3. middle	orange	Hub
1498	12	Alveolar membrane integrity loss (lungs)	2. cellular	3. middle	yellow	Hub
1535	63	Heart failure	4. organ	5. AO	red	
1549	67	Liver injury	4. organ	5. AO	red	other organs
1672	11	Lung surfactant function, decrease	3. tissue	3. middle	yellow	Lung
1678	48	Hypoxia	2. cellular	4. late	red	Hub
1706	73	Toll like receptors, dysregulation	1. molecular	2. early	green, orange	Hub
1738	new	Increased susceptibility to viral entry	1. molecular	2. MIE	green	Lung
1739	1	ACE2 receptor binding	1. molecular	1. MIE	green	Lung
1739	24	ACE2 receptor binding, sustentacular and basal cells	1. molecular	1. MIE	red	
1739	51	ACE2 receptor binding, pericytes	1. molecular	1. MIE	red	
1739	41	ACE2 receptor binding, endothelial cells	1. molecular	1. MIE	green	Hub
1740	8	ACE2 expression, decrease	1. molecular	2. early	green	Lung
1748	71	Acute respiratory distress syndrome (ARDS)	4. organ	5. AO	yellow, orange	Lung
1752	75	Angiotensin II, increased	1. molecular	2. early	red	
1787	8	ACE2 expression, decrease	1. molecular	2. early	green	Lung
1825	65	Cell death	2. cellular	2. early	yellow	Hub
1841	39	Encephalitis	4. organ	5. AO	red	Neuro
1842	73	Toll like receptors, dysregulation	1. molecular	2. early	green, orange	Hub
1843	71	Acute respiratory distress syndrome (ARDS)	4. organ	5. AO	yellow, orange, red	Lung

1844	22	Hyperinflammation / systemic inflammation	3. tissue	3. middle	orange, red	Hub
1845	13	Coagulation, increase	1. molecular	3. middle	orange, yellow	Hub
1846	49	Disseminated intravascular coagulation	3. tissue	5. AO	red	Hub
1846	58	Thrombosis	3. tissue	5. AO	orange, red	Hub
1847	new	Increased coronavirus production	1. molecular	2. early	green	Lung
1848	73	Toll like receptors, dysregulation	1. molecular	2. early	green, orange	Hub
1851	60	Angiotensin II, decreased	1. molecular	2. early	red	
1854	10	ACE2 dysregulation	1. molecular	2. early	orange, yellow, green	Hub
1857	21	Neutrophil-platelet interaction	2. cellular	3. middle	orange	Hub
1866	15	Fibrinolysis, decrease	1. molecular	3. middle	orange	Hub
1867	14	Bradykinin system, activated	1. molecular	3. middle	orange	Hub
1868	22	Hyperinflammation / systemic inflammation	3. tissue	3. middle	orange, red	Hub
1870	25	Sustentacular cells death	2. cellular	3. middle	red	
1871	26	Damage/death olfactory sensory neurons	2. cellular	3. middle	red	
1872	27	Olfactory epithelium degeneration	2. cellular	4. late	red	
1873	28	Anosmia	3. tissue/organ	5. AO	red	
1874	30	Disruption blood brain barrier	3. tissue	3. middle	red	
1875	52	Stroke / Cerebrovascular disease	4. organ/ 5.individual	5. AO	red	Neuro
	4	Translation Host/viral	1. molecular	2. early	green	Lung
	6	Viral replication	1. molecular	2. early	green	Lung
	59	Angiotensin 1-7, decreased	1. molecular	2. early	red	
	17	NLRP3 inflammasome, activation	1. molecular	3. middle	orange	Hub
	42	Tissue factor activation	1. molecular	3. middle	yellow, orange, red	Hub
	44	HMWK, increase	1. molecular	3. middle	yellow, orange, red	Hub
	46	Fibrin clot formation	1. molecular	3. middle	yellow, orange, red	Hub
	43	Endothelial cell disruption, prothrombotic expression	1. molecular/ 2. cellular	3. middle	yellow, orange, red	Hub
	50	Multi-organ failure	4. organ	5. AO	red	Hub
	47	Sepsis	5. individual	5. AO	red	Hub
	2	TMPRSS2 activation	1. molecular	2. early	green, red	Lung
	3	Neuropilin-1 binding	1. molecular	2. early	green	Lung
	5	Viral transcription	1. molecular	2. early	green	Lung
	9	RAS imbalance	1. molecular	2. early	green	Lung
	7	Innate immune evasion	1. molecular/ 2.cellular	2. early	green	Lung
	34	ACE2 receptor binding, mitral/tufted cells/astrocytes/pericytes	1. molecular	1. MIE	red	
	35	ACE2 receptor binding, olfactory epithelium	1. molecular	1. MIE	red	
	36	ACE2 receptor binding, CNS (endothelial, neuronal and glial cells)	1. molecular	1. MIE	red	
	64	ACE2 receptor binding, liver cells	1. molecular	1. MIE	red	
	68	ACE2 receptor binding, kidney cells	1. molecular	1. MIE	red	
	29	Sustentacular cells regeneration	2. cellular	3. middle	red	
	31	Regeneration olfactory neurons	2. cellular	3. middle	red	
	33	Neuroepithelial regeneration	2. cellular	3. middle	red	
	32	Neuroepithelial atrophy	2. cellular	4. late	red	
	55	Ischemia	3. tissue	4. late	red	
	56	Microvascular dysfunction	3. tissue	4. late	red	
	57	Coronary artery vasoconstriction	3. tissue	4. late	red	
	62	Myocardial injury	4. organ	4. late	red	
	40	MS (multiple Sclerosis)	4. organ	5. AO	red	

	38	Seizures / Epilepsy	5. individual	5. AO	red	
	74	Multi-scale KEs	6. multi-scale	6. several	orange	
	76	Intestinal permeability, increased	4.organ			other organs

Annex B: Some other interdisciplinary initiatives focusing on COVID-19

MPSCoRe	Microphysiological Systems for COVID-19 Research	https://nc3rs.org.uk/supporting-adoption-microphysiological-systems-covid-research
COVID-19 Map	Johns Hopkins Coronavirus Resource Center	https://coronavirus.jhu.edu/map.html
DRAGON	The Innovative Medicines Initiative DRAGON project	https://www.imi.europa.eu/projects-results/project-factsheets/dragon
COVID-19 Disease Map	The Disease Maps community	https://covid.pages.uni.lu/
COVID-19 Helix Community	CrowdHelix initiative	https://crowdHelix.com/helices/covid-19
COVID-19 Data Portal	The European COVID-19 Data Platform	https://www.covid19dataportal.org/