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COVID-19 and vertical transmission: assessing the expression of ACE2 / TMPRSS2 in the human fetus and placenta to assess the risk of SARS-CoV-2 infection.

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Abstract

Background: While pregnant women have been identified as a potentially at-risk group concerning COVID-19 infection, little is known regarding the susceptibility of the fetus to infection. Co-expression of ACE2 and TMPRSS2 has been identified as a pre-requisite for infection, and expression across different tissues is known to vary between children and adults. However, the expression of these proteins in the fetus is unknown. Methods: We performed a retrospective analysis of single cell data repositories. This data was then validated at both gene and protein level by performing qRT-PCR and two-colour immunohistochemistry on a library of second-trimester human fetal tissues. Findings: TMPRSS2 is present at both gene and protein level in the predominantly epithelial fetal tissues analysed. ACE2 is present at significant levels, only in the fetal intestine and kidney and is not expressed in the fetal lung. The placenta is also negative for the two proteins both during development and at term. Interpretation: This dataset indicates that the lungs are unlikely to be a viable route of SARS-CoV2 fetal infection. The fetal kidney, despite presenting both the proteins required for the infection, is anatomically protected from the exposure to the virus. However, the GI tract is likely to be susceptible to infection due to its high co-expression of both proteins, as well as its exposure to potentially infected amniotic fluid. Funding: This work was made possible by an MRC / UKRI COVID-19 Rapid response initiative grant (MR/V028480/1).

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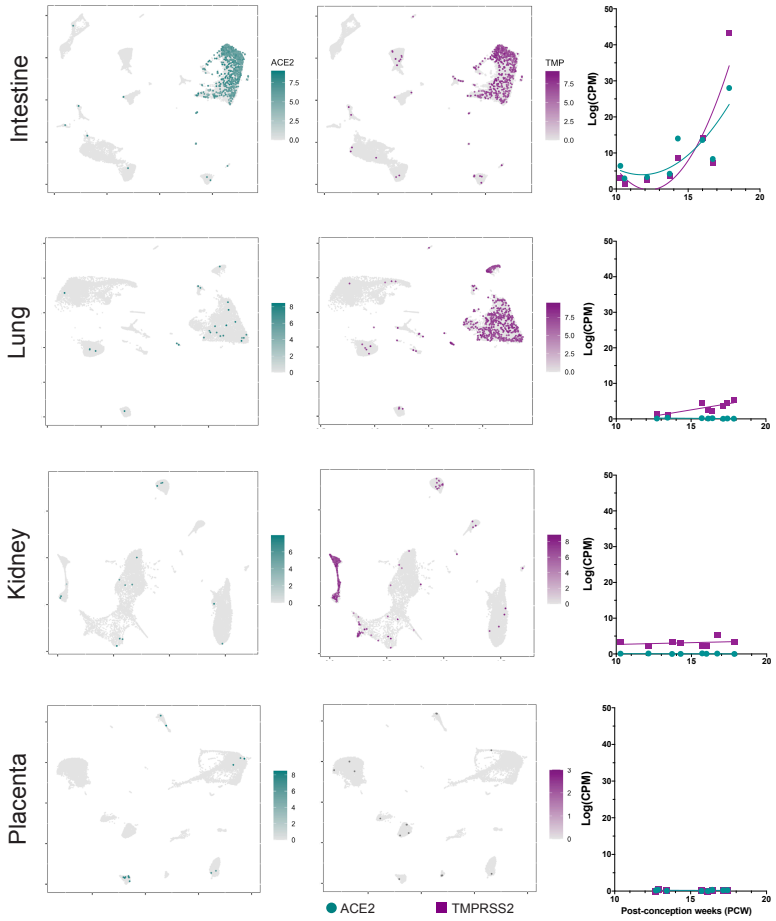

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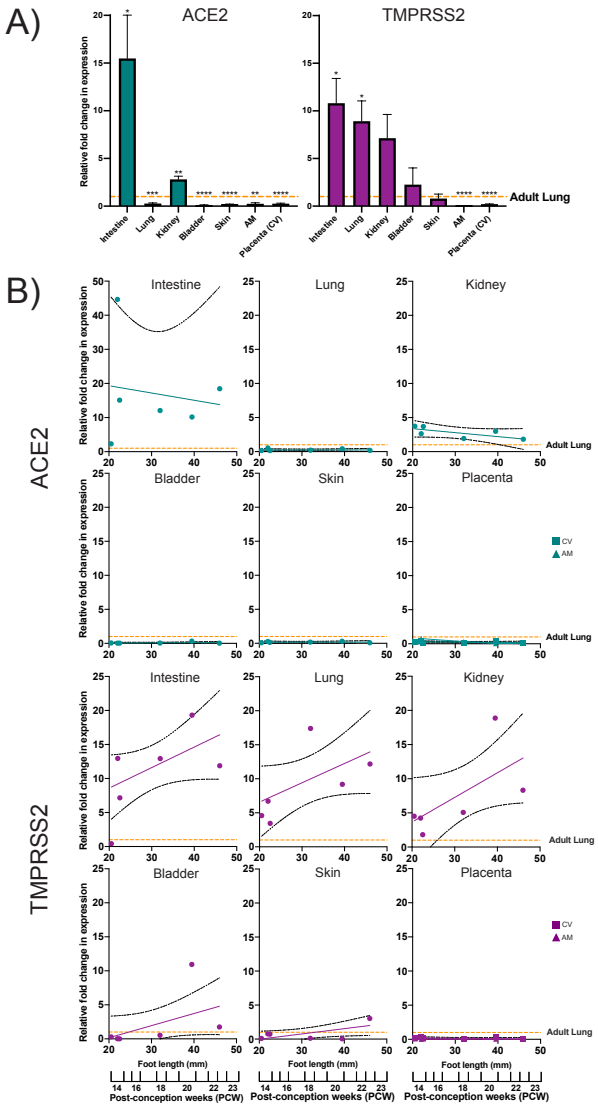

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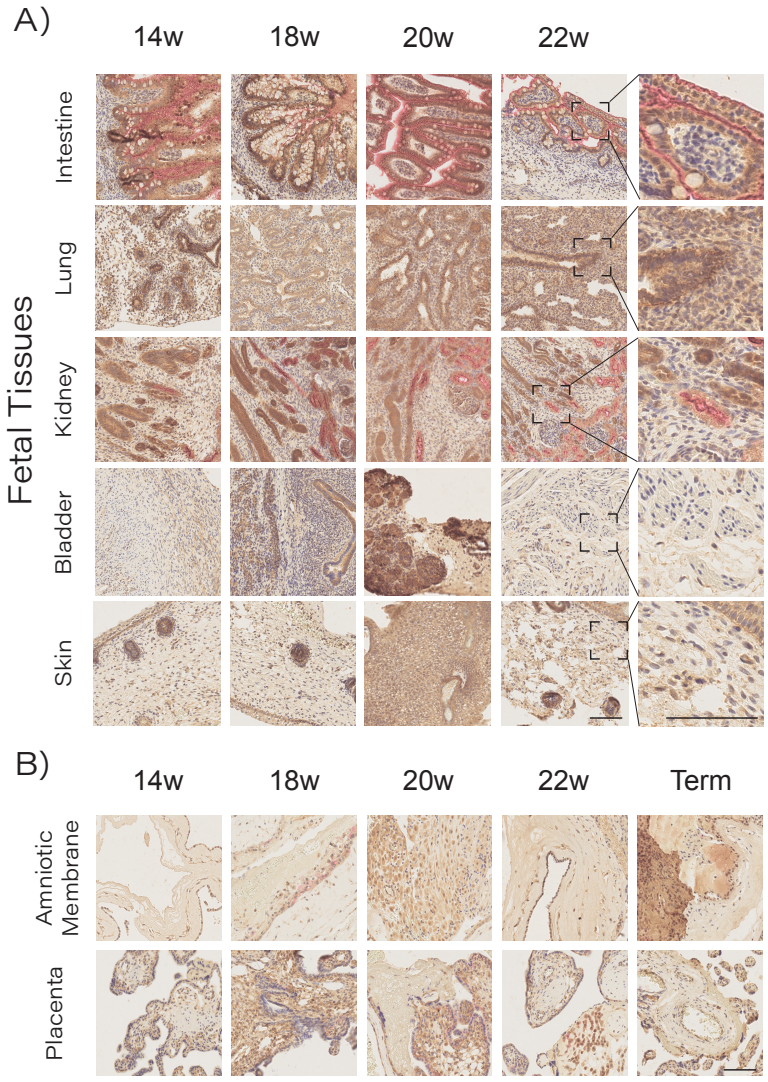

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Sample	ACE2											
	Mean	SD	SEM	N	t-Test vs Adult Lung	R^2	Mean	SD	SEM	N	t-Test vs Adult Lung	R^2
Intestine	15.49	11.13	4.54	6	p=0.0243	0.0240	10.80	6.39	2.61	6	p=0.0132	0.1420
Lung	0.28	0.16	0.07	6	p=0.0001	0.0002	8.92	5.22	2.13	6	p=0.0137	0.2087
Kidney	2.80	0.83	0.34	6	p=0.0031	0.1478	7.14	6.11	2.50	6	p=0.0573	0.2401
Bladder	0.09	0.12	0.05	6	p≤0.0001	0.0386	2.26	4.31	1.76	6	p=0.5071	0.1895
Skin	0.17	0.09	0.04	6	p≤0.0001	0.0005	0.80	1.14	0.47	6	p=0.6852	0.2511
Amniotic Membrane	0.25	0.27	0.11	6	p=0.0010	0.2268	0.03	0.03	0.01	6	p≤0.0001	0.0725
Placenta	0.25	0.12	0.05	6	p≤0.0001	0.0399	0.18	0.14	0.06	6	p≤0.0001	0.0888
Term Placenta	0.45	0.26	0.10	7	P=0.0013		0.28	0.11	0.04	7	p≤0.0001	

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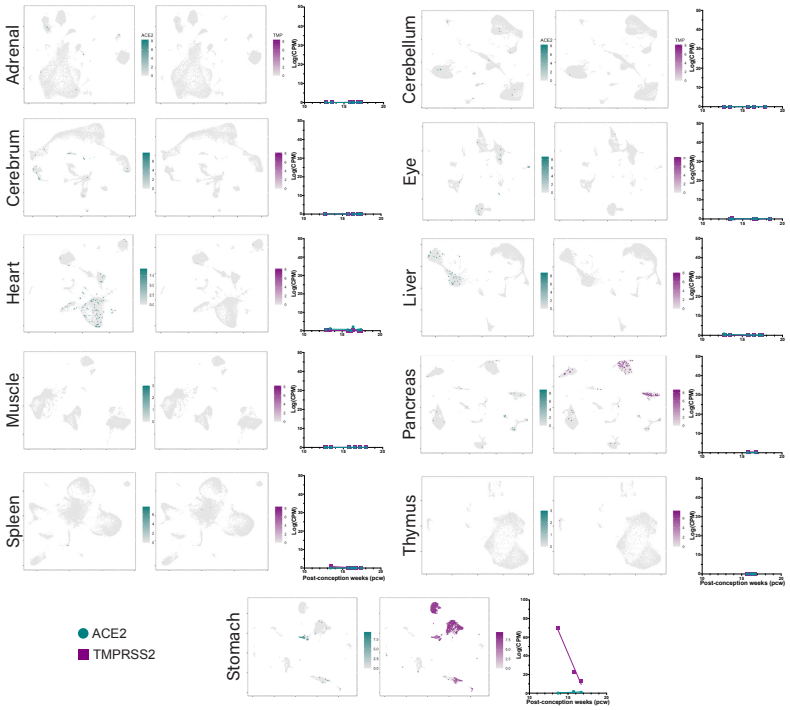
Sample	GA (PCW)	ACE2 (%)	TMPRSS2 (%)	Co-localisation (%)	Area (mm^2)
Intestine	14	9.2	24.4	1.2	53.4
	18	0.2	45.1	0.0	9.4
	20	15.3	25.3	2.8	109.3
	22	8.4	31.9	0.6	10.9
	Average	8.3	31.7	1.2	45.8
Lung	14	0.0	46.9	0.0	4.7
	18	0.0	24.6	0.0	31.6
	20	0.6	48.3	0.0	190.8
	22	0.0	27.0	0.0	49.6
	Average	0.2	36.7	0.0	69.2
Kidney	14	4.0	46.9	0.5	6.0
	18	3.1	38.6	0.4	32.9
	20	4.5	45.7	0.3	81.3
	22	1.9	21.3	0.1	75.3
	Average	3.4	38.1	0.3	48.9
Bladder	14	0.0	2.0	0.0	7.2
	18	0.0	8.5	0.0	8.1
	20	0.0	65.1	0.0	0.5
	22	0.0	2.4	0.0	50.0
	Average	0.0	19.5	0.0	16.5
Skin	14	0.0	12.7	0.0	3.4
	18	0.0	14.0	0.0	10.5
	20	0.0	51.2	0.0	10.4
	22	0.0	37.1	0.0	3.6
	Average	0.0	28.8	0.0	7.0
Amniotic Membrane	14	0.0	4.0	0.0	8.9
	18	1.2	3.2	0.0	32.7
	20	0.9	27.6	0.7	85.4
	22	0.0	10.1	0.0	17.3
	38+	0.1	16.2	0.0	10.4
	Average	0.6	14.3	0.2	36.5
Placenta	14	0.0	21.3	0.0	3.3
	18	0.4	13.0	0.1	19.1
	20	1.0	17.7	0.1	126.8
	22	0.5	9.4	0.0	78.9
	38+	0.4	14.7	0.0	37.2
	Average	0.6	13.7	0.1	65.5

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