

Progenitors from the central nervous system drive neurogenesis in cancer

Philippe Mauffrey¹, Nicolas Tchitchek^{2,7}, Vilma Barroca^{1,7}, Alexis-Pierre Bemelmans³, Virginie Firlej⁴, Yves Allory⁵, Paul-Henri Roméo⁶ & Claire Magnon^{1*}

¹UMR967 (Laboratoire Cancer et Microenvironnement ATIP/AVENIR-INSERM-CEA), Institut de Radiobiologie Cellulaire et Moléculaire, Institut de Biologie François Jacob, Direction de la Recherche Fondamentale, Paris, France. ²UMR1184 (INSERM-CEA-Université Paris Saclay), Infectious Diseases Models for Innovative Therapies, Institut de Biologie François Jacob, Direction de la Recherche Fondamentale, Paris, France. ³UMR9199 (CNRS-CEA-Université Paris-Saclay), Molecular Imaging Research CENTER, Institut de Biologie François Jacob, Direction de la Recherche Fondamentale, Paris, France. ⁴U955 (INSERM), Hôpital Henri Mondor-Université Paris-Est, Paris, France. ⁵Department of Pathology, Institut Curie, Paris, France. ⁶UMR967 (INSERM-CEA-Université Paris Diderot-Université Paris Saclay), Laboratoire Réparation et Transcription dans les Cellules Souches, Institut de Radiobiologie Cellulaire et Moléculaire, Institut de Biologie François Jacob, Direction de la Recherche Fondamentale, Paris, France. ⁷These authors contributed equally: Nicolas Tchitchek, Vilma Barroca. *e-mail: claire.magnon@cea.fr

Supplementary Table 1. Clinical and Pathological characteristics of men with benign hyperplasia or prostate cancer

Patient characteristics				Tumor characteristics				
#	Age (years)	Risk	PSA (ng/ml)	Date of the surgery	Gleason score	Pathological stage	#Invaded zones	Recurrence 0-/1+
1	67	BPH	17	2013	-	-	-	-
2	72	BPH	7.42	2013	-	-	-	-
3	58	BPH	1.42	2013	-	-	-	-
4	85	BPH	3.3	2013	-	-	-	-
5	63	BPH	4.5	2014	-	-	-	-
6	85	BPH	6	2013	-	-	-	-
7	72	BPH	-	2013	-	-	-	-
8	55	BPH	0.92	2013	-	-	-	-
9	71	BPH	5.37	2013	-	-	-	-
10	68	BPH	4.9	2013	-	-	-	-
11	62	BPH	27	2013	-	-	-	-
12	69	BPH	3.6	2013	-	-	-	-
13	63	BPH	6.6	2013	-	-	-	-
14	83	BPH	-	2014	-	-	-	-
15	76	BPH	6	2014	-	-	-	-
16	65	Low	6.25	2007	6	T2c	0	0
17	63	Low	5.31	2007	6	T2b	0	0
18	68	Low	5.75	2007	6	T2c	0	0
19	69	Low	6.4	2007	6	T2a	0	0
20	59	Low	5	2007	6	T2a	1	0
21	72	Low	10.23	2006	6	T2c	0	0
22	58	Low	6.09	2006	6	T2c	0	0
23	64	Low	3.9	2007	6	T2c	0	0
24	55	Low	4.34	2007	6	T2c	0	0
25	59	Low	3.83	2006	6	T2c	0	0
26	63	Low	5.3	2007	6	T3a	1	0
27	60	Low	4.2	2007	6	T2c	1	0
28	59	Low	1.7	2008	6	T2b	0	0
29	53	Low	4.6	2008	6	T2c	0	0
30	73	Low	6.37	2008	6	T2a	1	0
31	76	Low	4.54	2008	6	T2c	0	0
32	60	Low	3.5	2009	6	T2c	1	1
33	60	High	13	2006	7	T2a	0	0
34	66	High	9.98	2007	7	T2a	0	0
35	71	High	9.6	2006	8	T3b	2	0
36	71	High	3.9	2006	8	T3a	2	1
37	70	High	13.22	2006	8	T3a	2	1
38	63	High	10.32	2008	8	T3a	2	1
39	75	High	12.26	2008	8	T4	4	1
40	70	High	8.7	2008	8	T3b	3	1
41	53	High	2.9	2009	8	T3b	2	1
42	60	High	8.91	2009	8	T4	3	1
43	60	High	16	2009	8	T3a	1	1
44	66	High	15.95	2009	8	T3a	2	1
45	62	High	7.11	2007	9	T3a	1	0
46	70	High	45	2008	9	T3b	4	1
47	71	High	8.7	2008	9	T3b	4	0
48	50	High	12	2009	9	T3b	4	1
49	72	High	7.6	2007	9	T3b	2	0
50	74	High	4.5	2007	9	T3b	3	1
51	72	High	77.1	2006	9	T4	2	0
52	68	High	17.55	2006	9	T3a	2	0

Supplementary Table 2. Statistical comparisons of the number of DCX ⁺ cells between each type of human tissue			
Tissue type	P-value	95% lower CI	95% lower CI
Low (Normal) vs BPH	0.1678	-0.3000	1.8000
High (Normal) vs BPH	<0.0001	2.7000	11.4000
High (Normal) vs Low (Normal)	0.0001	2.3001	10.5000
Low (Tumour) vs BPH	0.4499	-3.5001	1.1999
High (Tumour) vs BPH	0.0001	6.1001	14.0000
High (Tumour) vs Low (Tumour)	<0.0001	7.7999	14.8001

Supplementary Table 3. Statistical comparisons of the number of DCX ⁺ cells relative to the number of invaded zones			
# Invaded zones vs 0 zone	P-value	95% lower CI	95% upper CI
1 zone	0.3507	-2.4	13.5
2 zones	0.0001	8.3	19.1
3 zones	0.0033	10.0	27.9
4 zones	0.0008	20.6	60.5

Supplementary Table 4. Correlations between the number of DCX ⁺ cells and the number of invaded zones				
Tissue type	Spearman coefficient	P-value	95% lower CI	95% upper CI
Normal	0.5825	1.55E-04	0.2870	0.8076
Tumour	0.7342	2.32E-07	0.5403	0.8540
Combined	0.7797	7.97E-09	0.5862	0.8832

Supplementary Table 5. Correlations between Immgen populations and the top 200 most expressed genes in each sample

Population group name	Population detailed name	SVZ 1		SVZ 2		OB 1		OB 2		Prostate 1		Prostate 2	
		R	p-value	R	p-value	R	p-value	R	p-value	R	p-value	R	p-value
B cell	Bone Marrow Common Lymphoid Progenitor	0.08	0.4698	0.09	0.4318	0.08	0.4662	0.05	0.6126	0.00	0.9790	-0.14	0.4318
B cell	Bone Marrow Fr. A (Pre-Pro-B)	0.09	0.4536	0.09	0.4453	0.09	0.4318	0.07	0.5404	-0.02	0.8365	-0.14	0.4318
B cell	Bone Marrow Fr. BC (Pro-B)	0.11	0.4318	0.12	0.4318	0.11	0.4318	0.08	0.4698	0.01	0.9563	-0.10	0.4318
B cell	Bone Marrow Fr. E (newly formed B)	0.12	0.4318	0.12	0.4318	0.12	0.4318	0.07	0.5292	0.01	0.9187	-0.11	0.4318
B cell	Splenic T1	0.11	0.4318	0.11	0.4318	0.11	0.4318	0.07	0.5229	0.04	0.7209	-0.11	0.4318
B cell	Splenic T2	0.11	0.4318	0.11	0.4318	0.10	0.4318	0.05	0.6285	0.02	0.8871	-0.10	0.4318
B cell	Splenic T3	0.11	0.4318	0.11	0.4318	0.10	0.4318	0.05	0.6163	-0.01	0.9563	-0.14	0.4318
B cell	Splenic B cells	0.11	0.4318	0.10	0.4318	0.10	0.4318	0.05	0.6126	0.01	0.9306	-0.10	0.4318
B cell	Female Splenic B cells	0.10	0.4318	0.10	0.4318	0.10	0.4318	0.05	0.6285	0.01	0.9488	-0.12	0.4318
B cell	Splenic Follicular	0.10	0.4318	0.10	0.4318	0.08	0.4698	0.03	0.7822	0.02	0.8961	-0.11	0.4318
B cell	Splenic Marginal Zone	0.09	0.4478	0.08	0.4698	0.09	0.4506	0.04	0.7545	0.02	0.8573	-0.11	0.4318
B cell	Splenic Memory	0.11	0.4318	0.10	0.4318	0.10	0.4318	0.04	0.7337	0.01	0.9319	-0.13	0.4318
B cell	Splenic Germinal Center Centroblasts	0.11	0.4318	0.10	0.4318	0.10	0.4318	0.06	0.6126	0.04	0.6997	-0.07	0.5166
B cell	Splenic Germinal Center Centrococytes	0.13	0.4318	0.12	0.4318	0.12	0.4318	0.08	0.4698	0.03	0.8026	-0.08	0.4662
B cell	Splenic Plasmablasts	0.08	0.4699	0.10	0.4318	0.06	0.5713	0.03	0.7770	0.01	0.9529	-0.07	0.5166
B cell	Splenic Plasma cells	0.07	0.5229	0.10	0.4318	0.08	0.4915	0.04	0.6802	-0.01	0.9557	-0.14	0.4318
B cell	Bone Marrow Plasma cells	0.11	0.4318	0.12	0.4318	0.11	0.4318	0.09	0.4425	0.02	0.8441	-0.12	0.4318
B cell	Peritoneal B1b	0.09	0.4434	0.09	0.4516	0.08	0.4698	0.02	0.8365	0.00	0.9859	-0.14	0.4318
ab T cells	Thymic preT DN1	0.07	0.5404	0.09	0.4478	0.09	0.4568	0.06	0.6015	-0.03	0.8141	-0.15	0.4318
ab T cells	Thymic preT DN2a	0.05	0.6163	0.07	0.5229	0.05	0.6126	0.04	0.7095	-0.04	0.7217	-0.17	0.4318
ab T cells	Thymic preT DN2b	0.06	0.6126	0.06	0.5644	0.05	0.6126	0.03	0.8138	-0.03	0.7692	-0.14	0.4318
ab T cells	Thymic preT DN3	0.07	0.5004	0.09	0.4506	0.07	0.5139	0.04	0.7095	-0.02	0.8555	-0.11	0.4318
ab T cells	Thymic preT DN4	0.08	0.4698	0.09	0.4453	0.07	0.5211	0.04	0.7012	-0.02	0.8555	-0.11	0.4318
ab T cells	Intermediate Single-Positive Thymocytes	0.07	0.5166	0.08	0.4698	0.07	0.5404	0.03	0.8015	0.00	0.9853	-0.09	0.4318
ab T cells	Double Positive Thymocytes	0.04	0.6930	0.06	0.5599	0.07	0.5364	0.03	0.7610	-0.02	0.8339	-0.12	0.4318
ab T cells	CD4+ Thymocytes	0.10	0.4318	0.10	0.4318	0.10	0.4318	0.06	0.5404	-0.02	0.8591	-0.14	0.4318
ab T cells	Splenic Naïve CD4+ T cells	0.10	0.4318	0.08	0.4658	0.10	0.4318	0.05	0.6163	-0.06	0.5534	-0.18	0.4318
ab T cells	Female Splenic Naïve CD4+ T cells	0.10	0.4318	0.08	0.4658	0.08	0.4698	0.02	0.8408	-0.05	0.6126	-0.17	0.4318
ab T cells	Splenic Activated CD4+ T cells, aCD3+CD40 18 hr	0.14	0.4318	0.13	0.4318	0.11	0.4318	0.08	0.4698	-0.07	0.5291	-0.15	0.4318
ab T cells	CD8+ Thymocytes	0.08	0.4662	0.08	0.4698	0.08	0.4698	0.04	0.7062	-0.02	0.8743	-0.15	0.4318
ab T cells	Splenic Naïve CD8+ T cells	0.09	0.4453	0.09	0.4496	0.10	0.4318	0.05	0.6126	-0.05	0.6126	-0.17	0.4318
ab T cells	Splenic Triple Negative CD8+ P14 T cells	0.08	0.4662	0.08	0.4698	0.08	0.4662	0.03	0.7808	-0.05	0.6645	-0.17	0.4318
ab T cells	Splenic CD8+ Terminal Effector, LCMV d7	0.09	0.4478	0.07	0.5404	0.07	0.5166	0.03	0.7945	-0.01	0.9306	-0.12	0.4318
ab T cells	Splenic CD8+ Memory Precursor, LCMV d7	0.11	0.4318	0.09	0.4318	0.10	0.4318	0.07	0.5281	0.00	0.9874	-0.12	0.4318
ab T cells	Gut IEL CD8+ , LCMV d7	0.11	0.4318	0.10	0.4318	0.13	0.4318	0.09	0.4318	-0.01	0.9202	-0.10	0.4318
ab T cells	Splenic CD8+ Central Memory, LCMV d180	0.07	0.5139	0.05	0.6163	0.08	0.4915	0.01	0.9001	-0.02	0.8721	-0.15	0.4318
ab T cells	Splenic CD8+ Effector Memory, LCMV d180	0.07	0.5166	0.05	0.6285	0.05	0.6126	0.01	0.9897	-0.01	0.9514	-0.14	0.4318
ab T cells	Splenic CD25hi Tregs	0.10	0.4318	0.09	0.4478	0.11	0.4318	0.07	0.5166	-0.07	0.5139	-0.19	0.4318
ab T cells	Colonic FoxP3+ Nrplo Tregs	0.11	0.4318	0.10	0.4318	0.12	0.4318	0.06	0.5707	-0.03	0.7822	-0.16	0.4318
ab T cells	Splenic Natural Killer T cells	0.10	0.4318	0.10	0.4318	0.09	0.4318	0.06	0.5743	-0.01	0.9202	-0.12	0.4318
ab T cells	Splenic Natural Killer T cells, LPS 3hr	0.13	0.4318	0.14	0.4318	0.12	0.4318	0.08	0.4662	-0.02	0.8555	-0.13	0.4318
ab T cells	Splenic Natural Killer T cells, LPS 18hr	0.10	0.4318	0.11	0.4318	0.10	0.4318	0.05	0.6126	-0.05	0.6303	-0.15	0.4318
ab T cells	Splenic Natural Killer T cells, LPS 3d	0.11	0.4318	0.11	0.4318	0.10	0.4318	0.06	0.6126	-0.01	0.9306	-0.13	0.4318
gd T cells	Vg2+ Scart2+ immature thymocytes	0.07	0.5364	0.06	0.5610	0.08	0.4736	0.03	0.7710	-0.01	0.9306	-0.12	0.4318
gd T cells	Vg2+ Scart2- immature thymocytes	0.08	0.4832	0.08	0.4662	0.08	0.4662	0.04	0.7156	-0.02	0.8743	-0.13	0.4318
gd T cells	Vg1.1+ Scart2- immature thymocytes	0.08	0.4915	0.08	0.4915	0.06	0.6126	0.01	0.9306	-0.02	0.8490	-0.14	0.4318
gd T cells	Vg2+ CD27-.LN	0.10	0.4318	0.08	0.4736	0.09	0.4536	0.03	0.7630	-0.01	0.9056	-0.16	0.4318
gd T cells	Vg2+ CD27+.LN	0.10	0.4318	0.09	0.4524	0.11	0.4318	0.05	0.6126	-0.03	0.8026	-0.16	0.4318
gd T cells	Vg1.1+ CD27+.LN	0.09	0.4318	0.09	0.4506	0.10	0.4318	0.04	0.6894	-0.03	0.7822	-0.17	0.4318
gd T cells	Total Splenic gdT cells	0.09	0.4318	0.09	0.4536	0.10	0.4318	0.06	0.5534	-0.02	0.8377	-0.13	0.4318
Stromal cells	Subcutaneous Lymph Node Blood Endothelial Cell	0.12	0.4318	0.11	0.4318	0.10	0.4318	0.05	0.6285	0.06	0.6015	-0.02	0.8490
Stromal cells	Subcutaneous Lymph Node Lymphatic Endothelial Cell	0.13	0.4318	0.15	0.4318	0.09	0.4318	0.05	0.6126	0.01	0.9041	-0.10	0.4318
Stromal cells	Subcutaneous Lymph Node	0.12	0.4318	0.13	0.4318	0.13	0.4318	0.08	0.4658	0.10	0.4318	-0.04	0.7012

Supplementary Table 6. Primer sequences used for PCR	
Mouse genes	Primer sequences
<i>GFAP</i> For	AACCGCATCACCATTCTGTGA
<i>GFAP</i> Rev	CCCGCATCTCCACAGTCTTTA
<i>GLAST</i> For	TCACCAGATTTGTGCTCCCC
<i>GLAST</i> Rev	CCGTGGCTGTGATGCTTATTG
<i>Sox2</i> For	ACAGCATGTCTACTCGCAG
<i>Sox2</i> Rev	AGTGGGAGGAAGAGGTAACCA
<i>Musashi-1</i> For	CCAGCCAAAGGAGGTGATGT
<i>Musashi-1</i> Rev	CAGCATCCCAATACCCAGCA
<i>Musashi-2</i> For	GACCTGTCGCCGATCTCTAC
<i>Musashi-2</i> Rev	TCAAAGGTCCAGCTATGCCG
<i>Prom1</i> For	CTGCGATAGCATCAGACCAAGC
<i>Prom1</i> Rev	CTTTTGACGAGGCTCTCCAGATC
<i>EGFR</i> For	CGTGGTGACAGATCATGGCT
<i>EGFR</i> Rev	CGACAGGGCCCATCACATT
<i>Mash1</i> For	TTCTTCAAGGGCTCTGCG
<i>Mash1</i> Rev	CGGCTCCACTCTCCATCTTG
<i>Nestin</i> For	GCCTGCTAGAAGACAAGACTCA
<i>Nestin</i> Rev	GAGGCCTCAATGAACCCTGG
<i>CD24</i> For	GCTCCTACCCACGCAGATTT
<i>CD24</i> Rev	CTGGTGGTAGCGTTACTTGGA
<i>NeuroD1</i> For	CCTTGCTACTCCAAGACCCAG
<i>NeuroD1</i> Rev	GCGTCTGTACGAAGGAGACC
<i>Myc</i> For	CCTCAGAGTGCATCGACCCC
<i>Myc</i> Rev	ACTCCGTCGAGGAGAGCAGA
<i>CK5</i> For	TCGAAACACCAAGCACGAGA
<i>CK5</i> Rev	CTTCAGCAATGGCGTTCTGG
<i>CK18</i> For	GATATCCGTGTCCCGCTCTG
<i>CK18</i> Rev	AGGCGATCGTTCAGGTCTTG
<i>Gapdh</i> For	GCATGGCCTTCCGTGTTT
<i>Gapdh</i> Rev	CCTGCTTCACCACCTTCTTGA