

Supplemental material

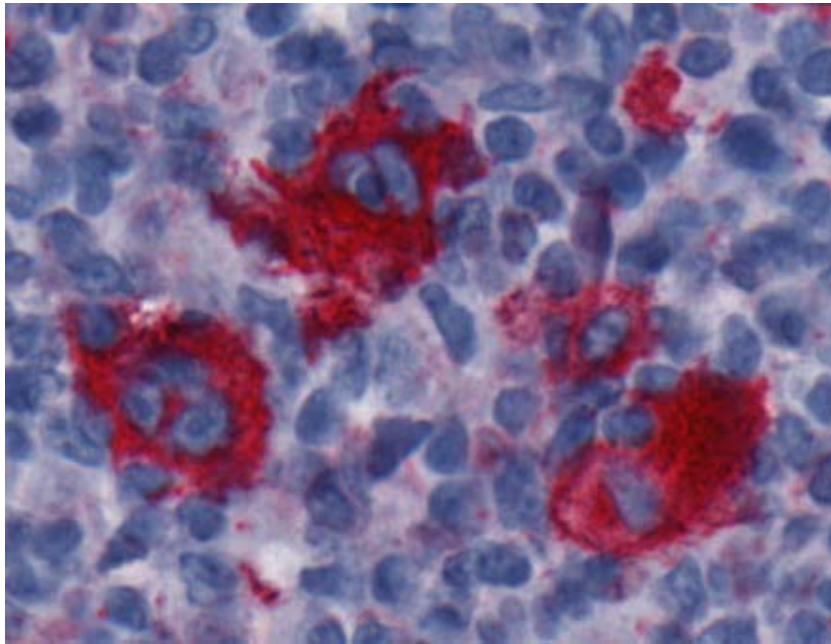


Figure S1: Cells with CD30-immunostaining are colored red. The cell nuclei are stained by hematoxylin and colored blue.

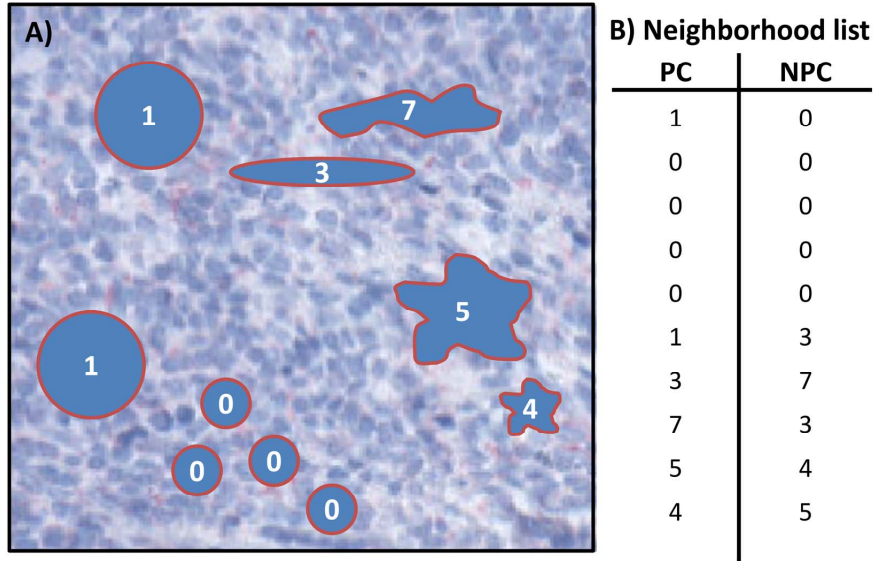


Figure S2: Example of a neighborhood list. A) The small sub-section of a histological image contains the profiles of ten CD30-positive cells. The number gives the corresponding profile class. B) The neighborhood list for the sub-section in A) has a row for each cell. The first column gives the profile class (PC) of the cell and the second column its nearest neighbor profile class (NPC).

A) 35 histological images								C) 12 histological images diagnosed as MCcHL									
	0	1	2	3	4	5	6	7		0	1	2	3	4	5	6	7
0	31 (89%)	-6 (17%)	4 (11%)	-3 (9%)	-15 (43%)	-18 (51%)	-26 (74%)	-18 (51%)	0	11 (92%)	1 (8%)	3 (25%)	1 (8%)	-6 (50%)	-6 (50%)	-8 (67%)	-5 (42%)
1	0	14 (40%)	-1 (3%)	7 (20%)	-6 (17%)	8 (23%)	-6 (17%)	8 (23%)	1	1 (8%)	3 (25%)	0	2 (17%)	-2 (17%)	1 (8%)	-3 (25%)	2 (17%)
2	5 (14%)	-1 (3%)	7 (20%)	1 (3%)	-3 (9%)	-5 (14%)	0	1 (3%)	2	2 (17%)	0	4 (33%)	1 (8%)	-3 (25%)	-2 (17%)	0	0
3	-1 (3%)	5 (14%)	0	6 (17%)	-4 (11%)	4 (11%)	-1 (3%)	2 (6%)	3	0	2 (17%)	0	2 (17%)	-2 (17%)	1 (8%)	-1 (8%)	1 (8%)
4	-9 (26%)	-8 (23%)	-4 (11%)	-6 (17%)	17 (49%)	-1 (3%)	9 (26%)	5 (14%)	4	-3 (25%)	-3 (25%)	-3 (25%)	-3 (25%)	7 (58%)	-1 (8%)	4 (33%)	-2 (17%)
5	-15 (43%)	10 (29%)	-2 (6%)	2 (6%)	1 (3%)	19 (54%)	-3 (9%)	20 (57%)	5	-5 (42%)	3 (25%)	-2 (17%)	1 (8%)	-1 (8%)	6 (50%)	-1 (8%)	7 (58%)
6	-24 (69%)	-8 (23%)	2 (6%)	-3 (9%)	9 (26%)	0	23 (66%)	3 (9%)	6	-7 (58%)	-3 (25%)	1 (8%)	-2 (17%)	4 (33%)	0	8 (67%)	-1 (8%)
7	-13 (37%)	6 (17%)	-1 (3%)	2 (6%)	-1 (3%)	15 (43%)	3 (9%)	15 (43%)	7	-4 (33%)	2 (17%)	-1 (8%)	1 (8%)	-1 (8%)	3 (25%)	-1 (8%)	5 (42%)
B) 12 histological images diagnosed as NScHL								D) 11 histological images diagnosed as LA									
	0	1	2	3	4	5	6	7		0	1	2	3	4	5	6	7
0	10 (83%)	-1 (8%)	0	-1 (8%)	-5 (42%)	-4 (33%)	-8 (67%)	-5 (42%)	0	10 (91%)	-6 (55%)	1 (9%)	-3 (27%)	-4 (36%)	-8 (73%)	-10 (91%)	-8 (73%)
1	1 (8%)	7 (58%)	0	3 (25%)	-3 (25%)	3 (25%)	-2 (17%)	3 (25%)	1	-2 (18%)	4 (36%)	-1 (9%)	2 (18%)	-1 (9%)	4 (36%)	-1 (9%)	3 (27%)
2	1 (8%)	-1 (8%)	2 (17%)	0	0	-2 (17%)	0	-1 (8%)	2	2 (18%)	0	1 (9%)	0	0	0	-1 (9%)	0
3	1 (8%)	1 (8%)	0	3 (25%)	-2 (17%)	1 (8%)	0	1 (8%)	3	-2 (18%)	2 (18%)	0	1 (9%)	0	2 (18%)	0	0
4	-2 (17%)	-3 (25%)	-1 (8%)	-3 (25%)	6 (50%)	-1 (8%)	2 (17%)	-3 (25%)	4	-4 (36%)	-2 (18%)	0	0	4 (36%)	1 (9%)	3 (27%)	0
5	-4 (33%)	3 (25%)	0	0	1 (8%)	6 (50%)	-1 (8%)	8 (67%)	5	-6 (55%)	4 (36%)	0	1 (9%)	1 (9%)	7 (64%)	-1 (9%)	5 (45%)
6	-7 (58%)	-4 (33%)	1 (8%)	-2 (17%)	4 (33%)	0	7 (58%)	1 (8%)	6	-10 (91%)	-1 (9%)	0	1 (9%)	1 (9%)	0	8 (73%)	3 (27%)
7	-2 (17%)	2 (17%)	0	1 (8%)	-1 (8%)	7 (58%)	1 (8%)	2 (8%)	7	-7 (64%)	2 (18%)	0	0	1 (9%)	5 (45%)	3 (27%)	7 (64%)

Figure S3: Score matrix. The score matrices show the scores of neighborhood relations for each combination of PC with respect to the diagnosis, A) all histological images, B) images of diagnosis NScHL, C) images of diagnosis MCcHL, and D) images of diagnosis LA. The values in the parentheses indicate the percentage of the score compared to the maximal, possible score. The score of a neighborhood relation gives a high positive value, if a combination of PC is *sh* in the majority of the images. All positive scores are highlighted green. Reversely, the score of a neighborhood relation gives a high negative value if a combination of PC is *sl* in most of the images. All negative scores are highlighted red.

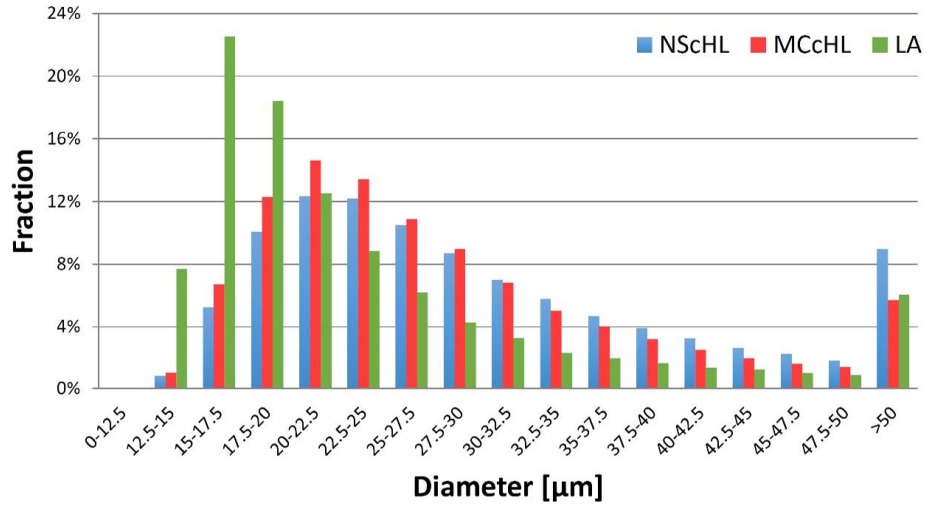
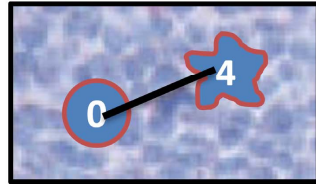


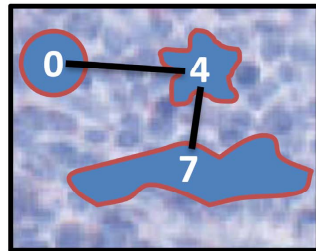
Figure S4: The distribution of diameters of cells. The bars show the relative fractions of cells versus the profile diameters for the diagnoses LA, NScHL, and MCcHL, respectively.

A) Symmetrical neighborhood relation



PC	NPC
0	4
4	0

B) Unsymmetrical neighborhood relation



PC	NPC
0	4
4	7
7	4

Figure S5: Symmetrical and unsymmetrical neighborhood relations. A) A geometrical arrangement of cells of a symmetrical neighborhood relation ($PC = 4$, $NPC = 0$) and *vice versa* ($PC = 0$, $NPC = 4$), and the corresponding neighborhood list. B) A geometrical arrangement of cells of an unsymmetrical neighborhood relation ($PC = 0$, $NPC = 4$) and ($PC = 4$, $NPC = 7$), and the corresponding neighbor list.

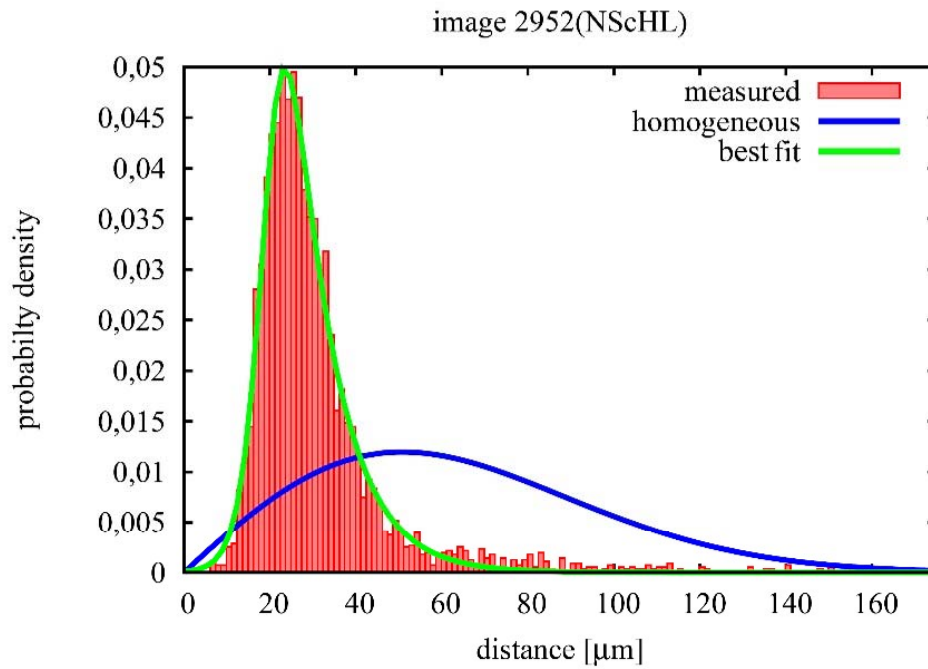


Figure S6: Distribution of distances of CD30-positive cells in an image of the diagnosis NScHL. The measured distribution (red bars) is much more narrow than expected from a spatially homogeneous random model (blue line). The green line is the best fit of a three-parameter density function (Roberts-Baranyi model) of the measured distribution. Similar results were found for all other images of the diagnosis NScHL.

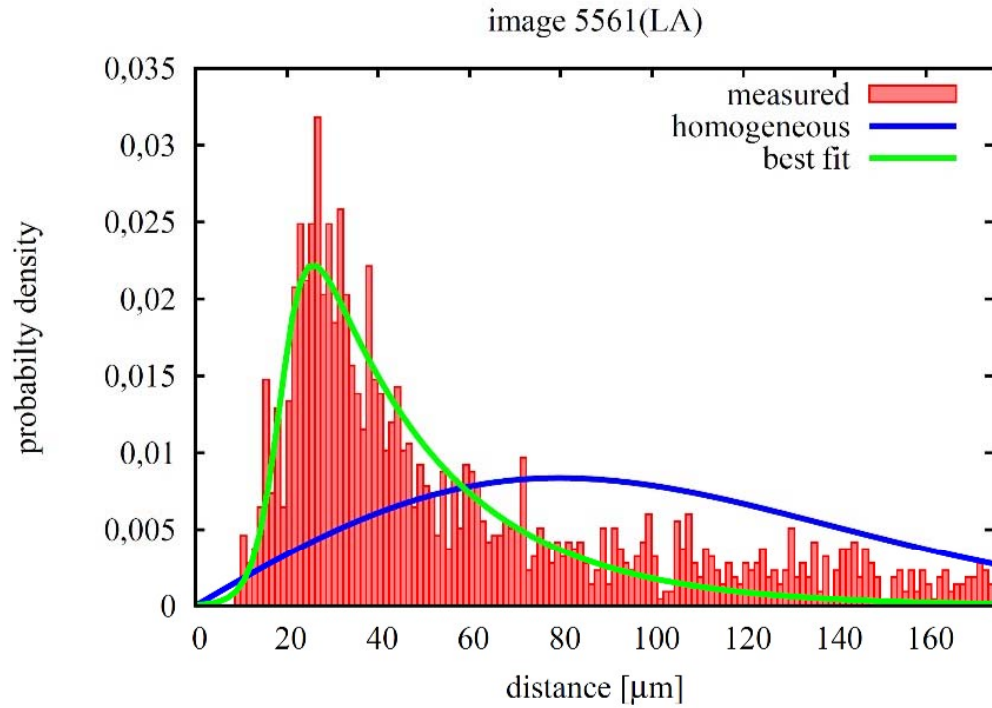


Figure S7: Distribution of distances of CD30-positive cells in an image of the diagnosis LA. The measured distribution (red bars) is much more narrow than expected from a spatially homogeneous random model (blue line). The green line is the best fit of a three-parameter density function (Roberts-Baranyi model) to the measured distribution. Similar results were found for all other images of the diagnosis LA.

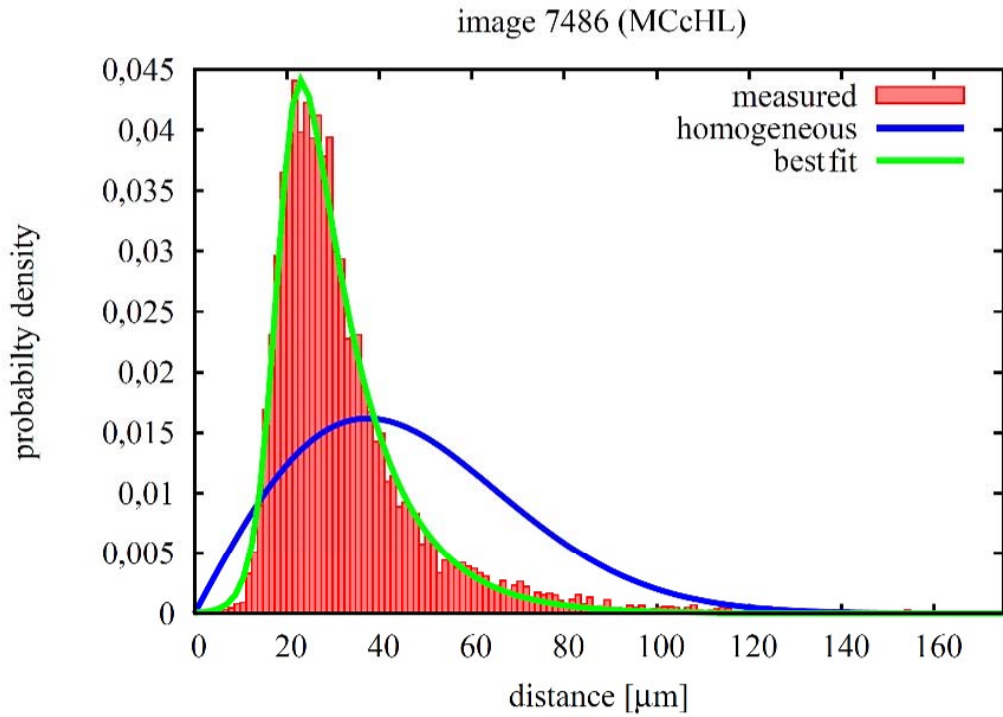


Figure S8: Distribution of distances of CD30-positive cells in an image of the diagnosis MCcHL. The measured distributions (red bars) is much more narrow than expected from a spatially homogeneous random model (blue line). The green line is the best fit of a three-parameter density function (Roberts-Baranyi model) to the measured distribution. Similar results were found for all other images of the diagnosis MCcHL.

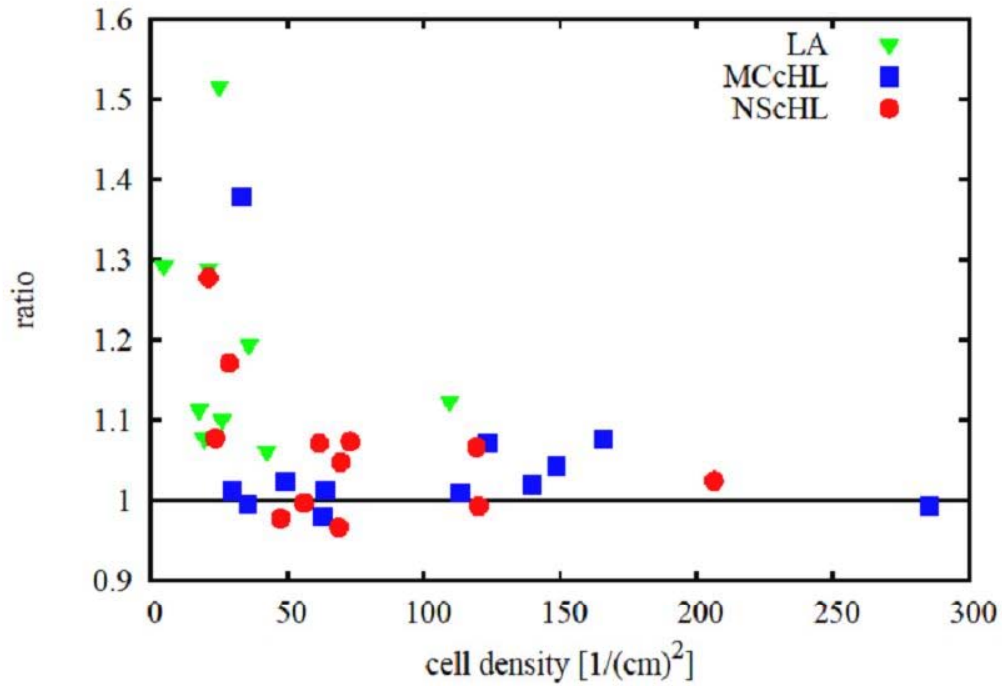


Figure S9: Ratios of mean distance of neighbors of $PC = 0$, i.e., cells with small, round profiles, to the mean distance of neighbors of arbitrary PC . For all WSI, the ratios are slightly above or around the value of 1. Despite the preferences of small, round cells to have a small, round neighbor, the distances of such pairs are not smaller than between other pairs. Consequently, an attraction between small, round cells is not the reason for the clustering of cell profiles of $PC = 0$. More likely, the location of small, round cells in tissue regions, which are either not easily accessible or deserted by other cell types, is the reason for the neighborhood between small, round cells. A high motility combined with a small size may lead to an aggressive ability of small, round cells to colonize still healthy tissue regions.

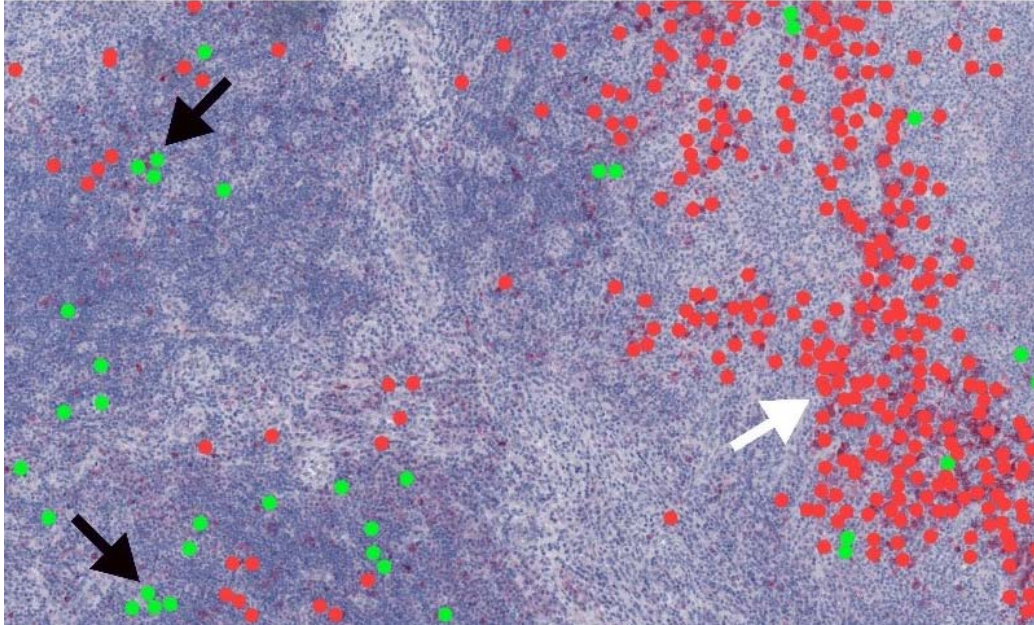


Figure S10: The sub-section of a histological image diagnosed as MCcHL (ID 5722). The green points depict small, round cells ($PC = 0$) with a nearest neighbor of the identical class, $NPC = 0$. The red points are all other cells. $PC = NPC = 0$ pairs are more often located in areas of low cell density (black arrows) than in areas of high cell density (white arrow).