

Figure 1

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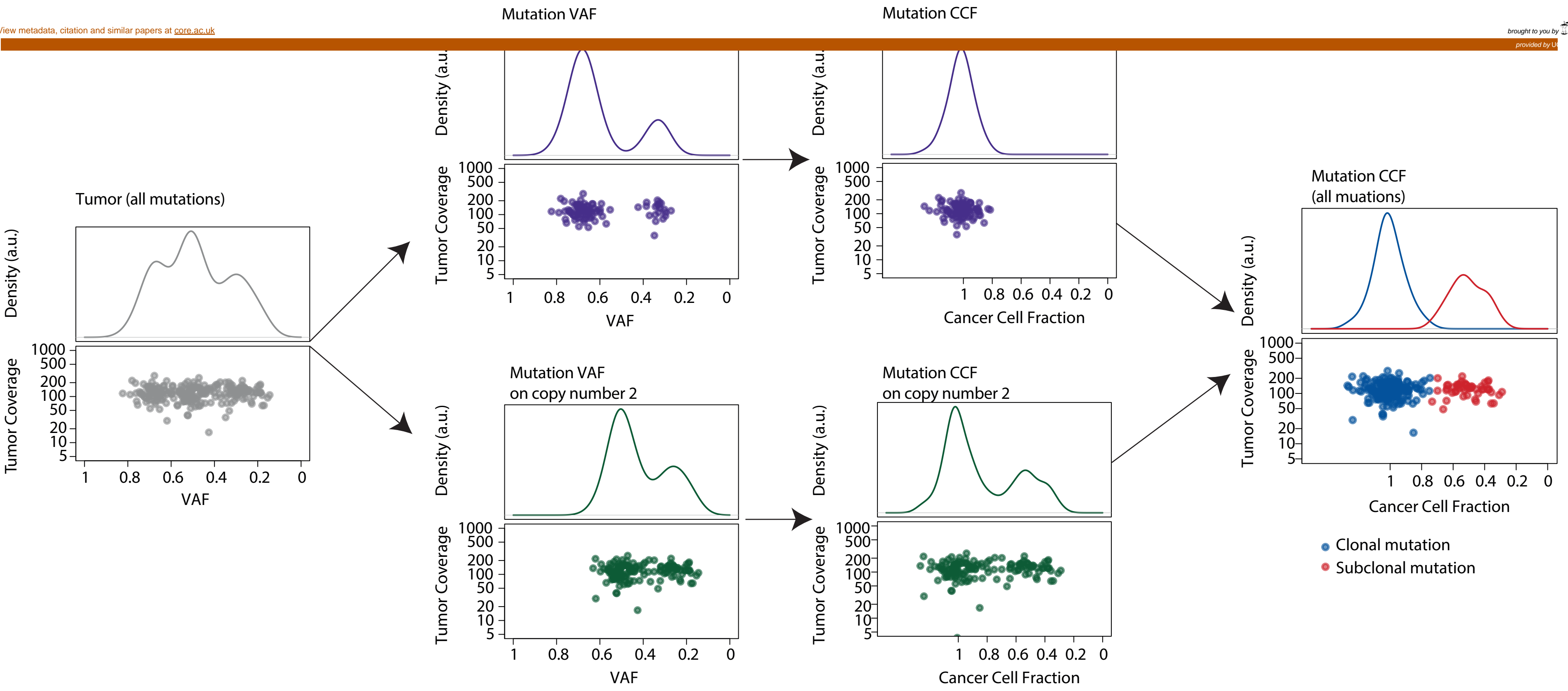
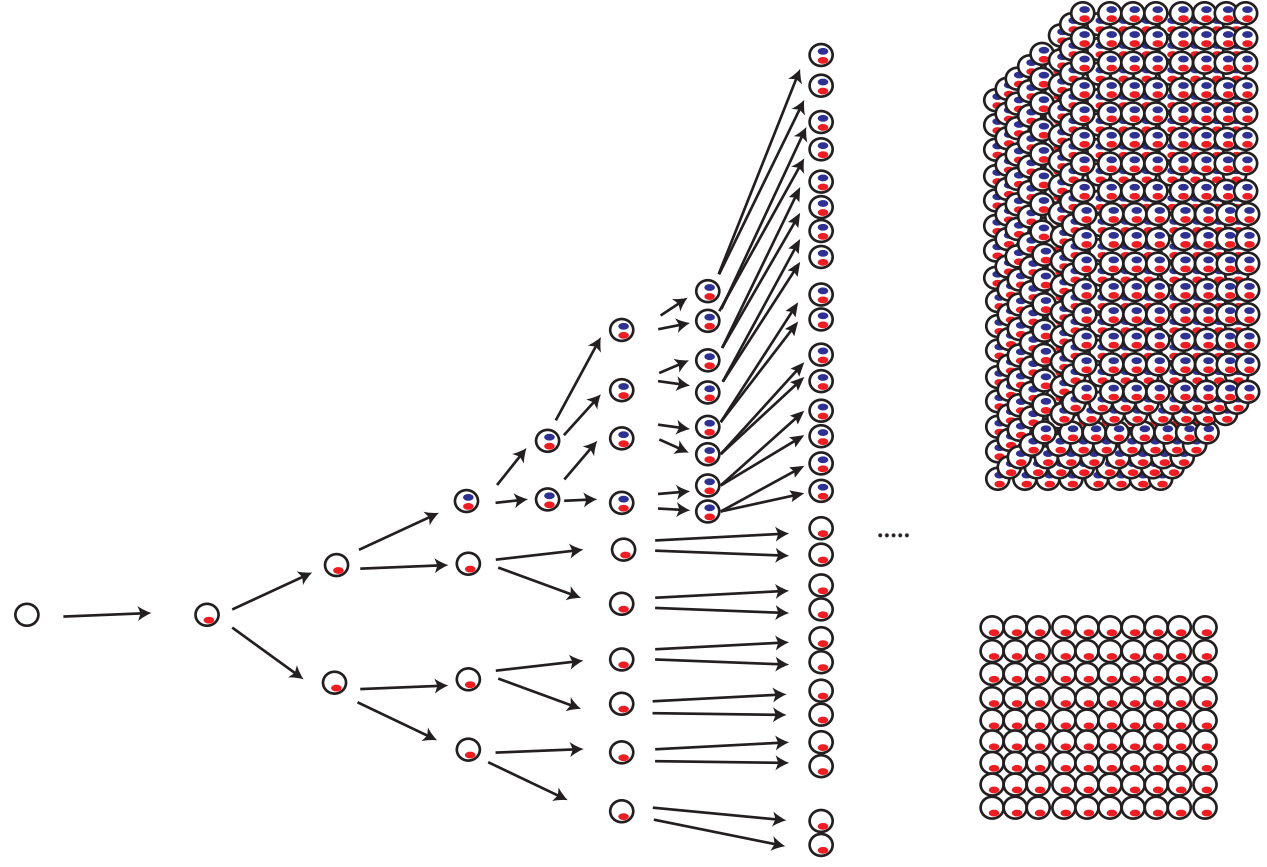


Figure 2

A) Mutations under positive selection

○	cellular frequency	0/1	1/1	2/2	4/4	5/5	10/10	14/14	28/28	640/640
	VAF	0.0	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
⊙	cellular frequency	0/1	0/1	0/2	1/4	2/5	4/10	8/14	16/28	620/640
	VAF	0.0	0.0	0.0	0.13	0.2	0.2	0.24	0.24	0.48



B) Mutations under neutral evolution

⊙	cellular frequency	0/1	1/1	2/2	4/4	8/8	16/16	640/640
	VAF	0.0	0.5	0.5	0.5	0.5	0.5	0.5
⊙	cellular frequency	0/1	0/1	0/2	1/4	2/8	4/16	160/640
	VAF	0.0	0.0	0.0	0.13	0.13	0.13	0.13
⊙	cellular frequency	0/1	0/1	0/2	0/4	0/8	1/16	40/640
	VAF	0.0	0.0	0.0	0.0	0.0	0.03	0.03

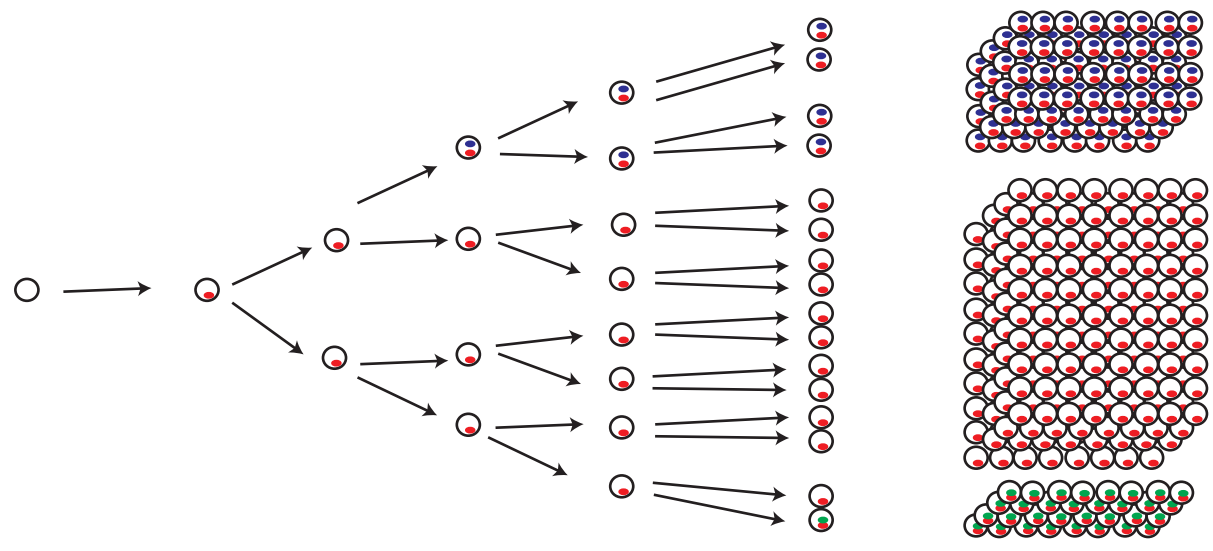
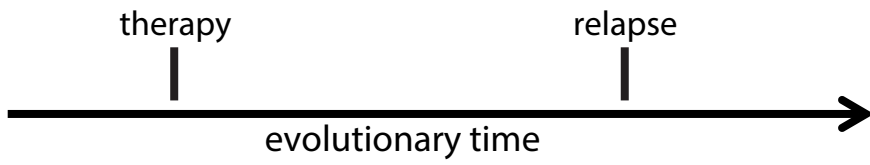
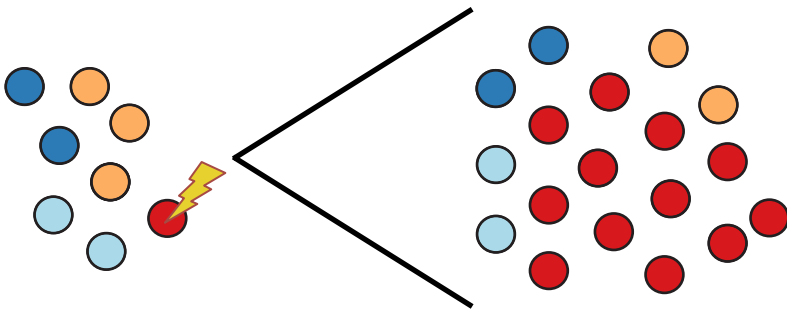


Figure 3

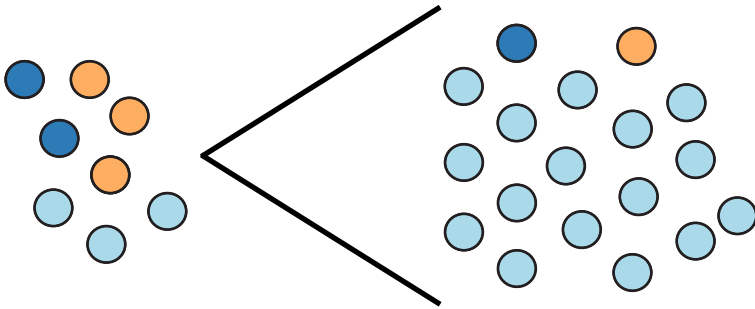


A) Therapy induced mutagenesis

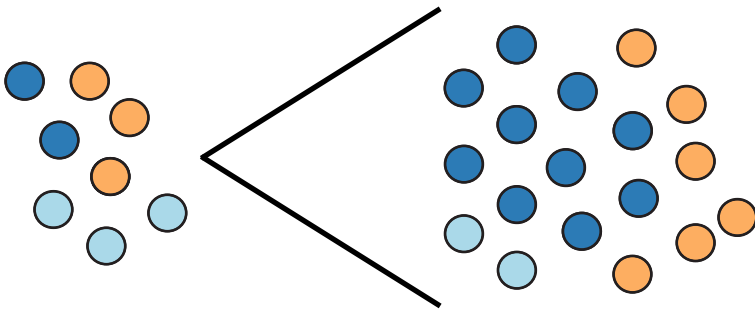


Therapy as a selective pressure

B) Pre-existing resistant clone



C) Shift in clonal composition



D) Maintenance of clonal composition

