Selection: Hydroxyurea (YPD+HU 10 mg/ml) WAXNA F12 1 HU 1 WAXNA F12 1 HU 2 WAXNA F12 1 HU 3 0.8 0.8 Cumistive subclone frequency, f. (bars) 0.6 0.4 0.2 subclone A subclone B subdone C 0.0 subclone D WAXNA F12 2 HU 1 WAxNA F12 2 HU 2 WAXNA F12 2 HU 3 Mutation 1.0 - driver non-synonymous 0.8 synonymous Oumulative subclone frequency, f. (bars) 0.6 0.6 0.4 0.4 0.2 0.2 2 4 8 16 32 Time, f (days) Selection: Rapamycin (YPD+RM 0.025 µg/ml) WAXNA F2 1 RM 1 WAXNA F12 1 RM 1 WAXNA F12 1 RM 2 WAXNA F12 1 RM 3 WAXNA F12 1 RM 4 1.0 0.8 0.8 Cumulative subdone frequency, ((bars) 0.6 0.4 (lines) 0.4 0.2 0.0 2 2 32 2 8 WAxNA F2 1 RM 2 WAXNA F12 2 RM 1 WAxNA F12 2 RM 2 WAXNA F12 2 RM 3 WAxNA F12 2 RM 4 1.0 0.8 0.8 0.6 0.6 0.4 0.4 0.2 0.2 8 Time, ridays)