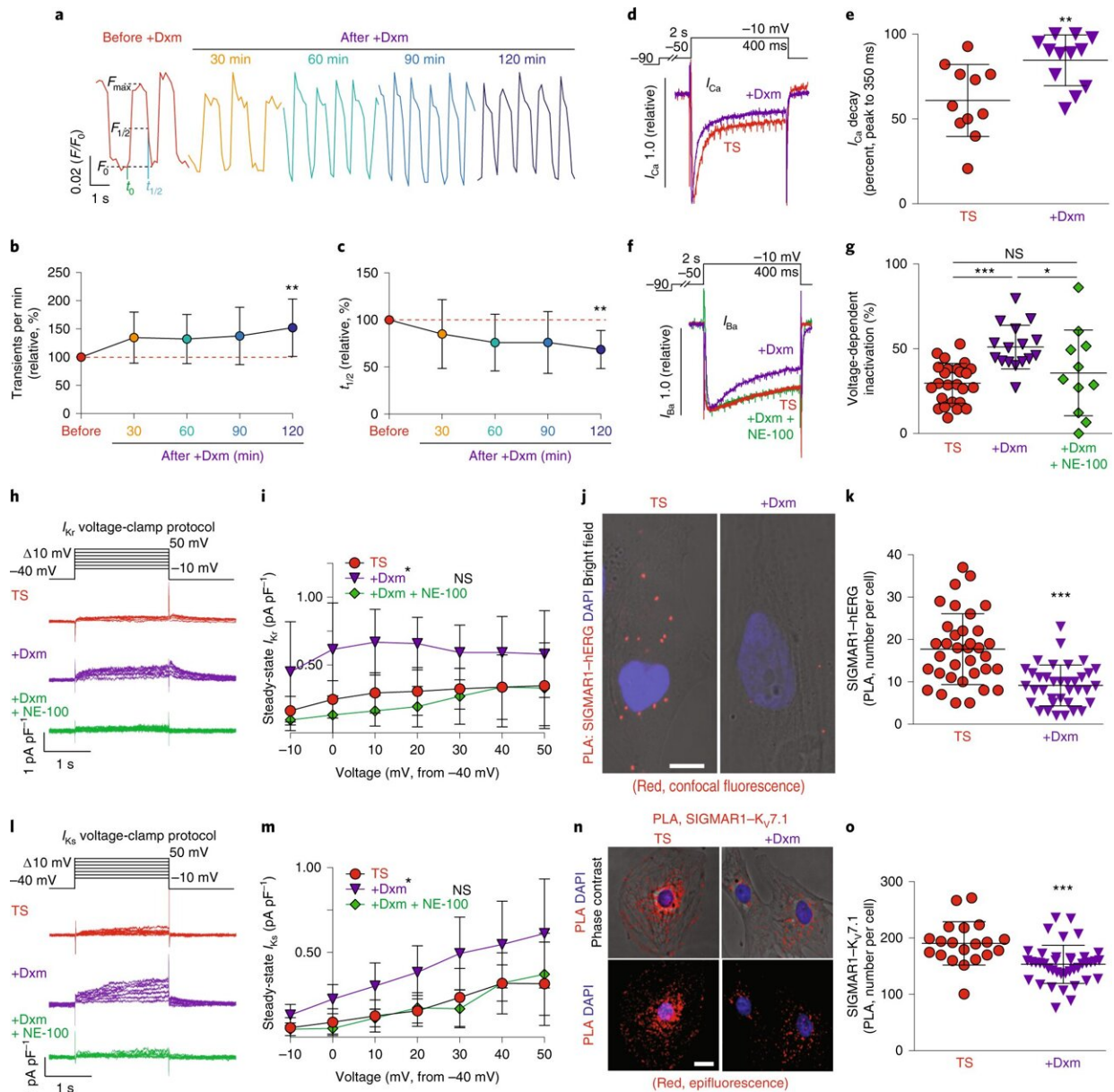


# Cough suppressant knocks some hearts back into rhythm

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The effect of dextromethorphan on cardiac  $\text{Ca}^{2+}$  handling and ion channels in a human iPSC model of TS. a, Representative traces of time-course  $\text{Ca}^{2+}$  imaging in spontaneously contracting cardiomyocytes from patients with TS treated with dextromethorphan ( $5 \mu\text{M}$ , until 120 min). b,c,  $\text{Ca}^{2+}$  transient frequency (b) and duration (c) analyses of cardiomyocytes from patients with TS before and after dextromethorphan treatment ( $n = 19$ ). d, Representative traces of  $\text{Ca}^{2+}$  currents in cardiomyocytes from patients with TS with and without dextromethorphan. e, Late  $\text{Ca}^{2+}$  current analysis of cardiomyocytes from patients with TS with and without dextromethorphan treatment (TS,  $n = 11$ ; with dextromethorphan,  $n = 12$ ). f, Representative traces of  $\text{Ba}^{2+}$  currents in cardiomyocytes from patients with TS without treatment or treated with dextromethorphan ( $5 \mu\text{M}$ , 2 h, dextromethorphan) or with dextromethorphan and a SIGMAR1 antagonist, NE-100 ( $1 \mu\text{M}$ , dextromethorphan and NE-100). g, Voltage-dependent inactivation in cardiomyocytes from patients with TS without treatment ( $n = 25$ ) or treated with dextromethorphan ( $n = 16$ ) or with dextromethorphan and NE-100 ( $n = 11$ ). h, Representative traces of  $\text{IKr}$  currents (E-4031 sensitive) in cardiomyocytes from patients with TS treated with dextromethorphan ( $5 \mu\text{M}$ ) or dextromethorphan and NE-100 (each at  $5 \mu\text{M}$ ) or without treatment. i,  $\text{IKr}$  current amplitude analysis of cardiomyocytes from patients with TS treated with dextromethorphan ( $n = 9$ ) or dextromethorphan and NE-100 ( $n = 10$ ) or without treatment ( $n = 10$ ) (\*P

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