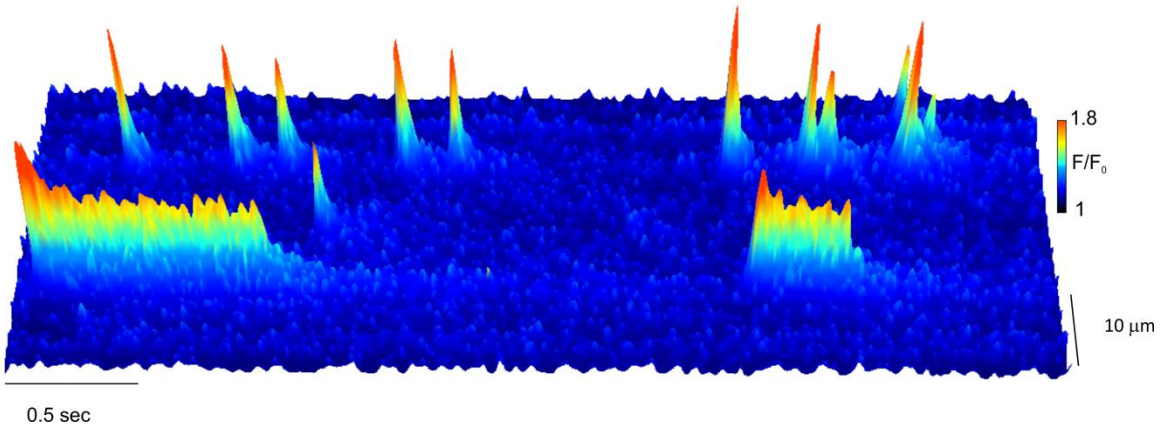

Figure S1 Ca^{2+} sparks and prolonged juxtanuclear Ca^{2+} release events are of similar amplitude. Surface plot of line scan image showing many brief Ca^{2+} sparks and 2 prolonged Ca^{2+} release events arising at the end of one of the nuclei in ARVMs. Similar results were recorded in cells from 4 hearts.

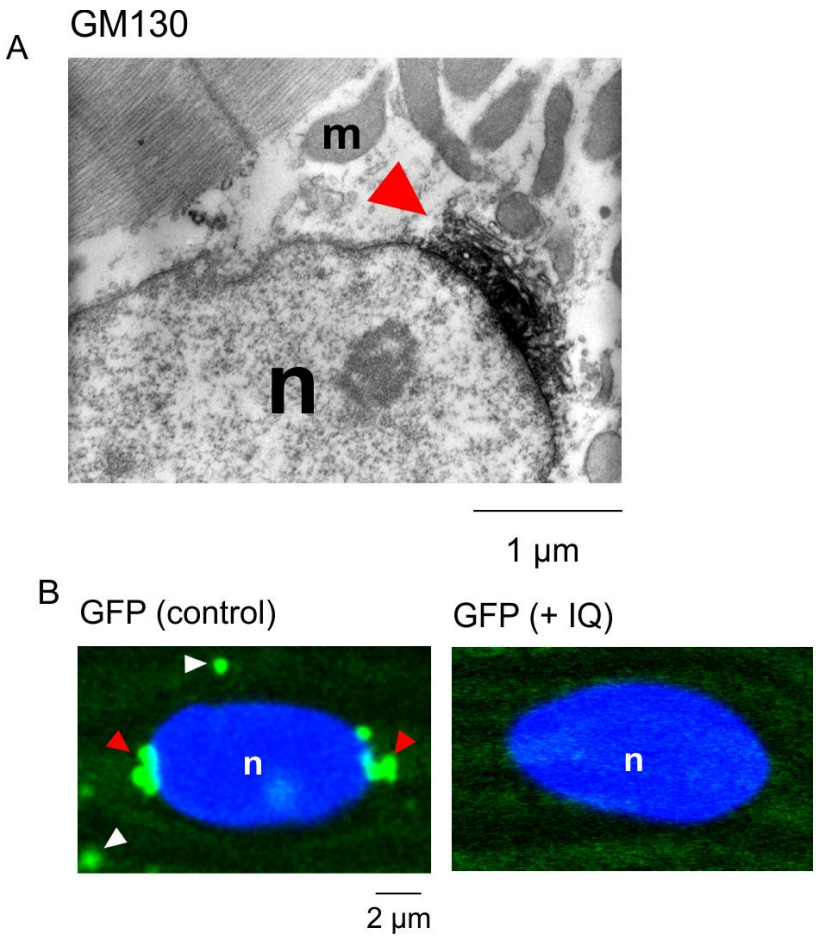

Fig. S2. The Golgi Apparatus is consistently located at the nuclear poles and can be disrupted by IQ. (**A)** Electron micrograph showing the location of the Golgi apparatus (*red arrow)* highlighted using DAB staining of the Golgi apparatus protein GM130. Mitochondria (m) and the nucleus (n). 'mf' indicates myofibrils are indicated. Similar results were seen cells from 2 hearts. **(B)** DAPI staining of the nucleus and expression of GFP targeted to the Golgi apparatus, highlighting the organelle at the nuclear poles (*red arrows*) and also cytosolic transfer vesicles *(white arrow)*. After pre-incubation with IQ, neither the Golgi apparatus nor the cytosolic vesicles were detectable *(right)*. Similar results were obtained cells from 4 hearts.

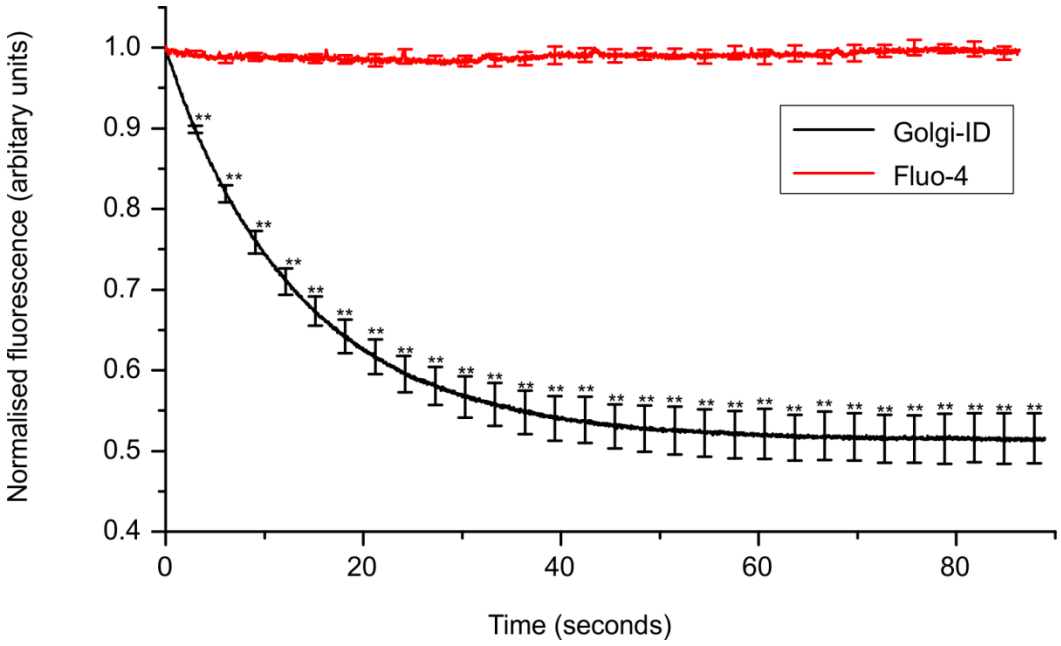

Fig. Golgi ID green fluorescence bleaches rapidly Cells loaded with either fluo-4 or Golgi-ID green were subjected to confocal imaging at the same laser intensity used in all other experiments. The Golgi ID fluorescence exhibited a rapid decrease, with a half time of approximately 15 sec, while the fluo-4 fluorescence did not change significanlty. At all time points beyond zero, the fluo-4 and Golgi-ID signals were significantly different * $p<0.01$, n=4 cells from 3 hearts.

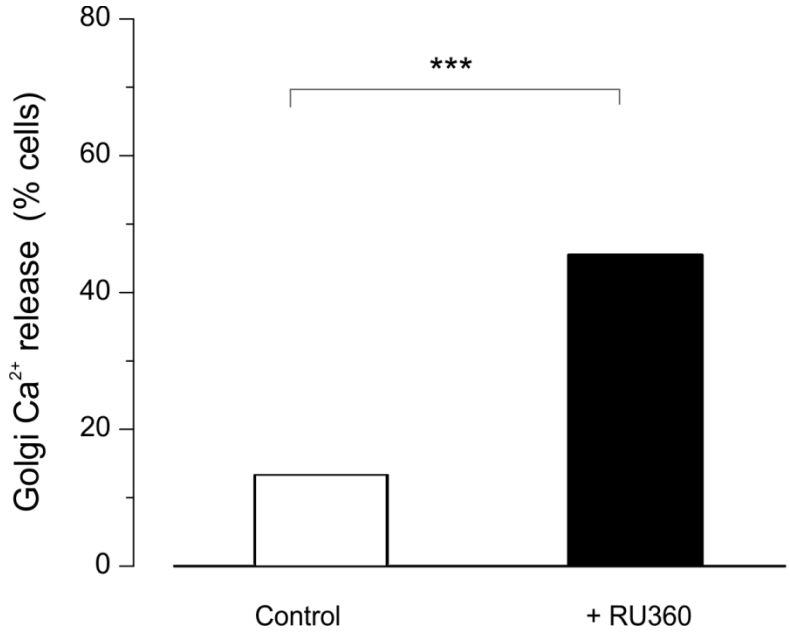

Fig. S4 RU360 stimulates Golgi Ca^{2+} release at the nuclear poles Cells loaded with Fluo-4 were imaged using line-scan confocal microscopy to detect Golgi Ca^{2+} release events. Inclusion of the mitochondrial Ca^{2+} uptake inhibitor RU360 caused a significant increase in the percentage of cells exhibiting Golgi Ca^{2+} release. (n=23 cells) Data were obtained from 3 hearts. *** P<0.01

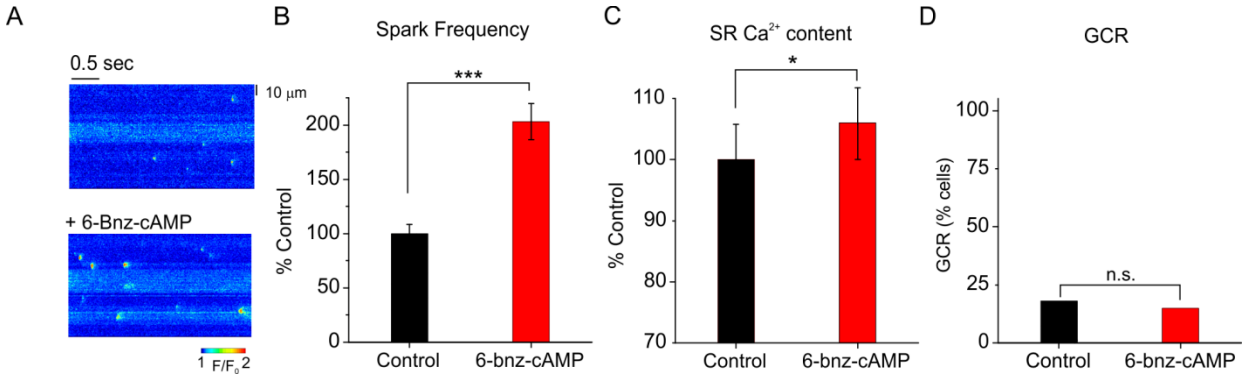

Fig. S5 6-bnz-cAMP stimulates SR Ca^{2+} sparks but not GCR (*A*) Original line-scan images showing Ca^{2+} sparks under control conditions (upper) and after exposure to the PKA activator 6-Bnz-cAMP. (*B*) Mean data showing that exposure to the selective PKA inhibitor 6-bnz-cAMP approximately doubled spark frequency (n=21 cells). (*C*) 6-bnz-cAMP significantly increased the SR Ca^{2+} content, as assessed by application of caffeine (n=18 cells). (*D*) 6-bnz-cAMP had no significant effect on the percentage of cells exhibiting Golgi Ca^{2+} release (GCR) within a 3 minute line scan (n=6 cells). Data were obtained from 3 hearts. *p<0.05, *** p<0.001.

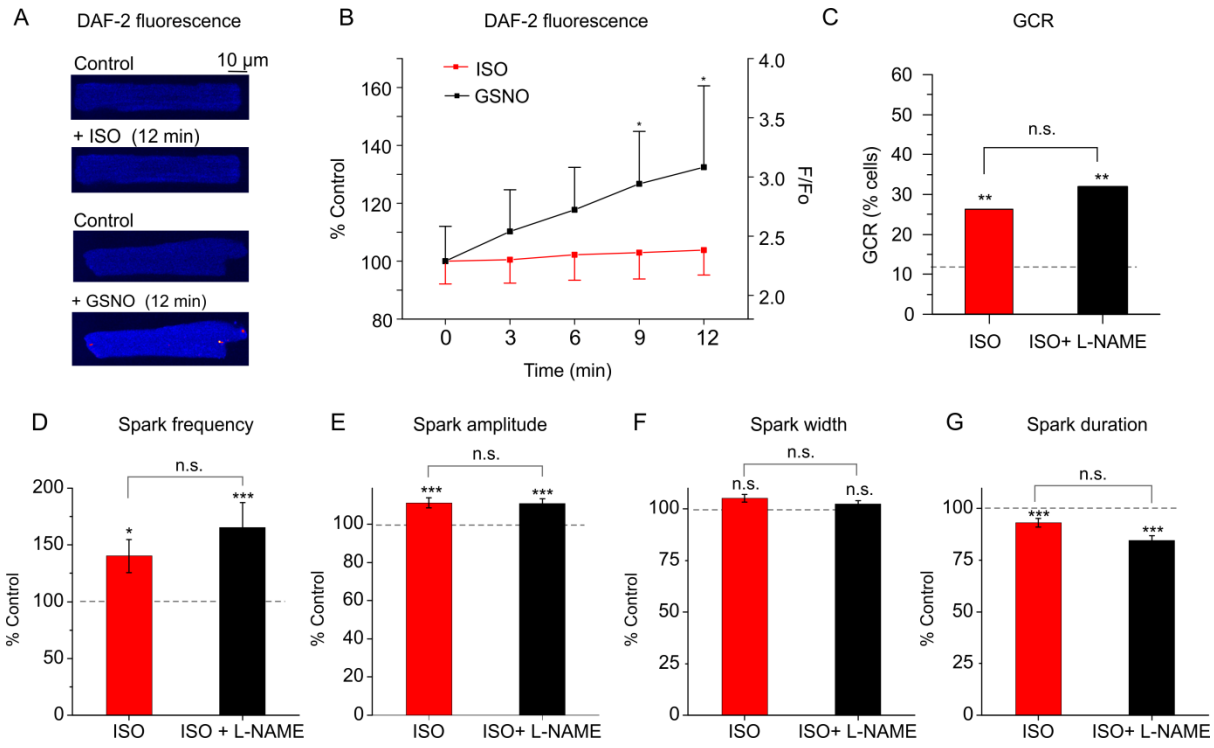

Fig. S6 Effects of ISO are not mediated by an increase in cytosolic NO (*A*) x-y confocal images showing DAF-2 (5 µM) fluorescence loaded ARVMs. A 12 min exposure to a high ISO concentration (10 µM) had no significant effect (*upper pair*), while exposure to the NO donor GSNO (500 µM) increased DAF-2 fluorescence. (*B*) mean data showing changes in DAF-2 fluorescence following addition of ISO or GSNO. Changes were corrected for small time dependent decreases min DAF-2 fluorescence due to bleaching. (n=19-20 cells) (C) 60 minutes pre-treatment with the NOS inhibitor L-NAME (500 µM) failed to prevent the stimulating effect of 1 µM ISO on Golgi Ca^{2+} release (GCR, n=19-25). (D-G) Similarly, L-NAME failed to prevent the stimulating effect of 1 µM ISO on SR Ca^{2+} spark frequency, amplitude, width or duration (n=11-16). Cumulative data were obtained from 3 hearts. Broken line indicates the control level in the absence of ISO or ISO+L-NAME. *p<0.05, ** p<0.01, ***, p<0.005.

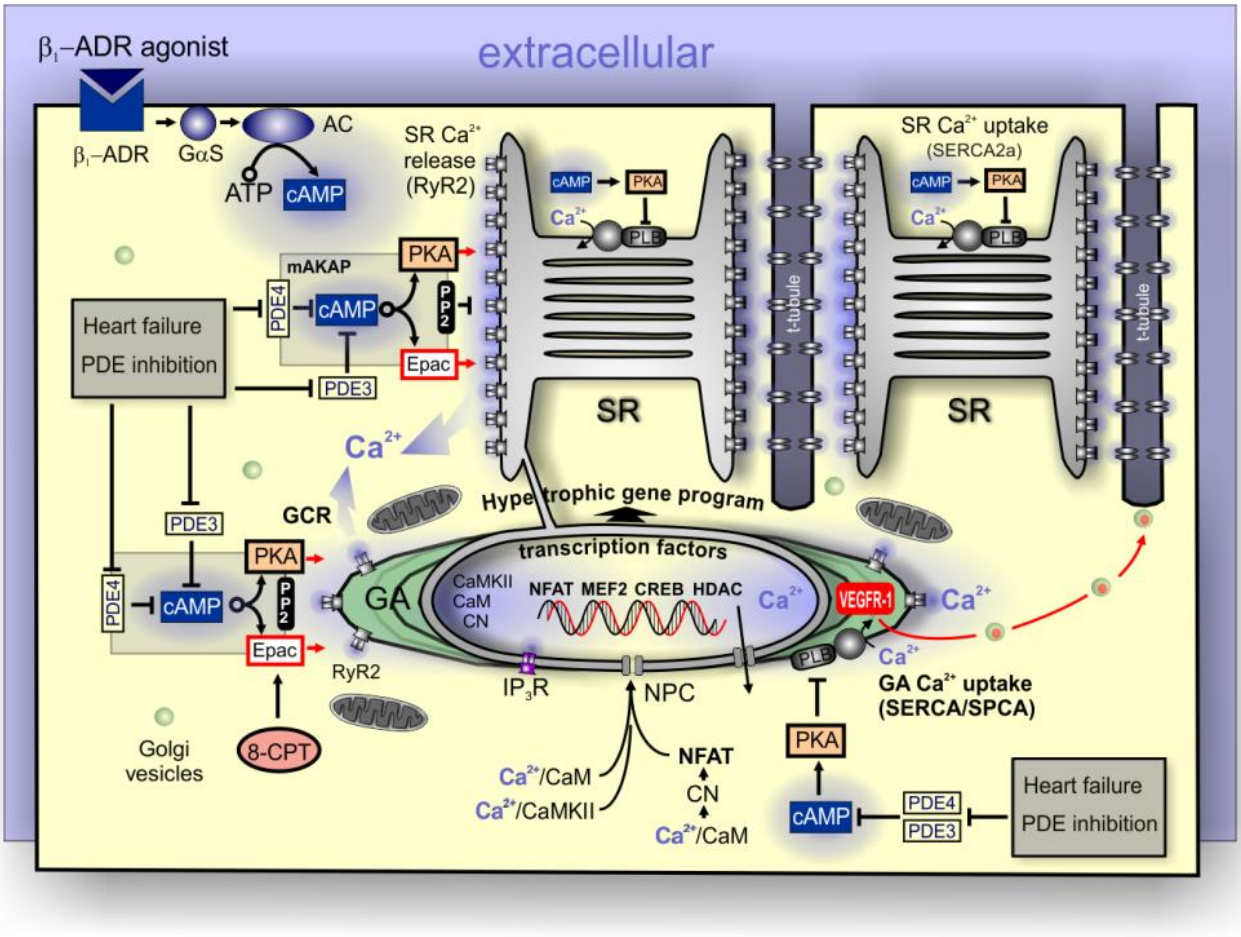

Fig. S7 Proposed mechanisms underlying β-adrenergic regulation of SR and GA function in ARVMs A single nucleus is shown with the lumen of nuclear envelope continuous with that of the SR. Nuclear pore complexes (NPC) allow ions and small molecules to pass between the nucleoplasm and the cytosol. GA stacks are located at the nuclear poles and secretory vesicles are present within the cytosol. RyR2 mediates Ca^{2+}-release from the junctional SR and the GA but is absent from the nuclear envelope in ARVMs. $InsP_3Rs$ are present in the nuclear envelope. Local [cAMP] is tightly controlled by tethered signaling complexes incorporating PDE4, membrane bound PDE3 and protein phosphatase (pp2). Under control conditions, β_1-AD agonists have only a small stimulating effect on GA Ca^{2+} signaling. However, when PDE 3 or 4 is inhibited or downregulated in HF, a local increase in [cAMP] leads to activation of Epac and stimulation of GCR via a CaMKII dependent mechanism. Factors that stimulate GA Ca^{2+} cycling facilitate movement of VEGFR-1 from the GA to the sarcolemma/t-tubules. Local Ca^{2+}-release from the $InsP_3Rs$ and the GA may contribute to Ca^{2+} dependent activation of transcription factors, including MEF2 and NFAT.