Supplemental Text

1. The bioactivity for G-protein activation by the three cDNAs (#1-8, #3-52, and #4-57) was also examined in β-galactosidase reporter assays with the different yeast strains. The three cDNAs (#1-8, #3-52, and #4-57) increased β-galactosidase activity in the yeast strain expressing Gα16 but not in yeast strains expressing Gαi3, Gαs or Gpa1.

2. The level of expression of TFEB in yeast was less than that of TFE3 or MITF and it is not clear if this lower expression accounted for its lack of activity in the yeast system when compared to the activity observed with the partial TFEB cDNA encoding the carboxyl terminus or whether the full-length protein contains regulatory domains that influence the bioactivity of the carboxyl terminus region.

3. Deletion of the C-terminus 27 amino acids did not affect the level of TFE3 expression in cells; however, the expression of TFEB was markedly reduced by deletion of the C-terminus.

Figure Legends for Supplemental Figures

Supplemental Figure 1. Cardiac hypertrophy induced by TAC or isoproterenol. The cardiac hypertrophy was developed in the mouse heart as described in the "Experimental Procedures". The wet wight of left ventricle (LV), body weight (BW), and tibial length were measured. Data were expressed in the ratio of the left ventricle to body weight(A, C) or to the tibial length (B,D) in mouse model of TAC or continuous infusion of isoproterenol (ISO). *p< 0.05.

Supplemental Figure 2. Localization of expressed Gα16 subunits in COS7 cells. *A-C,* COS7 cells were transfected in a 35-mm dish with 2.0 μg of Gα16 subunit in pcDNA3, 2.0 μg, pcDNA3.1-His::TFE3 or pcDNA3.1-His::deltaTFE3 as described in Figure 5 or 6B. The amount of transfected DNA was adjusted to 4 μg per well with the pcDNA3 vector. The Gα16 subunit and TFE3 were determined using a specific antibody for each Gα (red) or Xpress antibody (green), respectively. Arrow indicates the absence (A) or presence (B, C) of nuclear localization of Gα16. *D*, Effect of TFE3 on localization of Gα16 in COS7 cells. The number of cells expressing Gα16 and cells expressing Gα16 in the nucleus were counted, resepectively. Data are represent 160-200 transfected cells from 4-5 of independent experiments. Please note that ~40% of Gα16-transfected cells expressed TFE3 in double transfection of Gα16 and TFE3 constructs. Thus, typically, 60-70% of Gα16-TFE3 expressing cells showed nuclear localization of Gα16. *p<0.05 vs Gα16 group.