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| **Table S3: Statistics for WT versus variant values** |
| **Construct** | **Agonist** | **Modulator** | **EC50 (µM)** | **P** | **Emax (Fold)** | **P** | **Assay** | **Figure** |
| WT | Nateglinide | - | 23.02 | 0.096 | 123.90 | <0.001 | PRESTO-Tango | 1C |
| N245S+ T43T | 10.06 | 42.49 | 1D |
| WT | Nateglinide | - | 15.30 | 0.87 | 3.42 | 0.01 | PI Hydrolysis  | 1D |
| N245S+ T43T | 13.33 | 1.92 | 1D |
|  |  |  |  |  |  |  |  |  |
| P values were calculated via F-test comparing statistical difference between either EC50 or Emax values between WT and variant. |