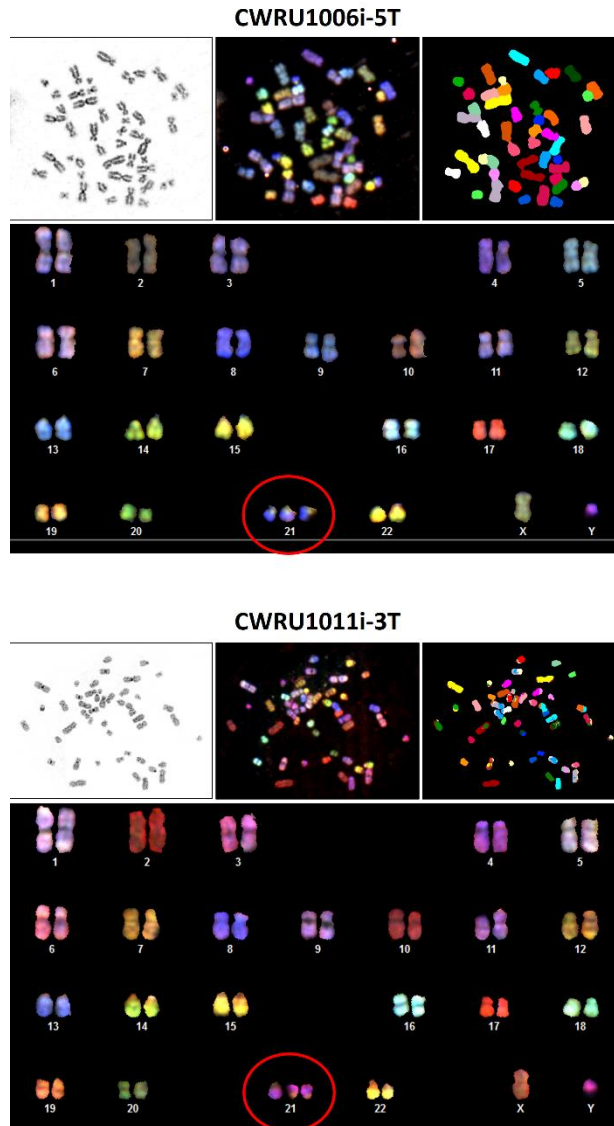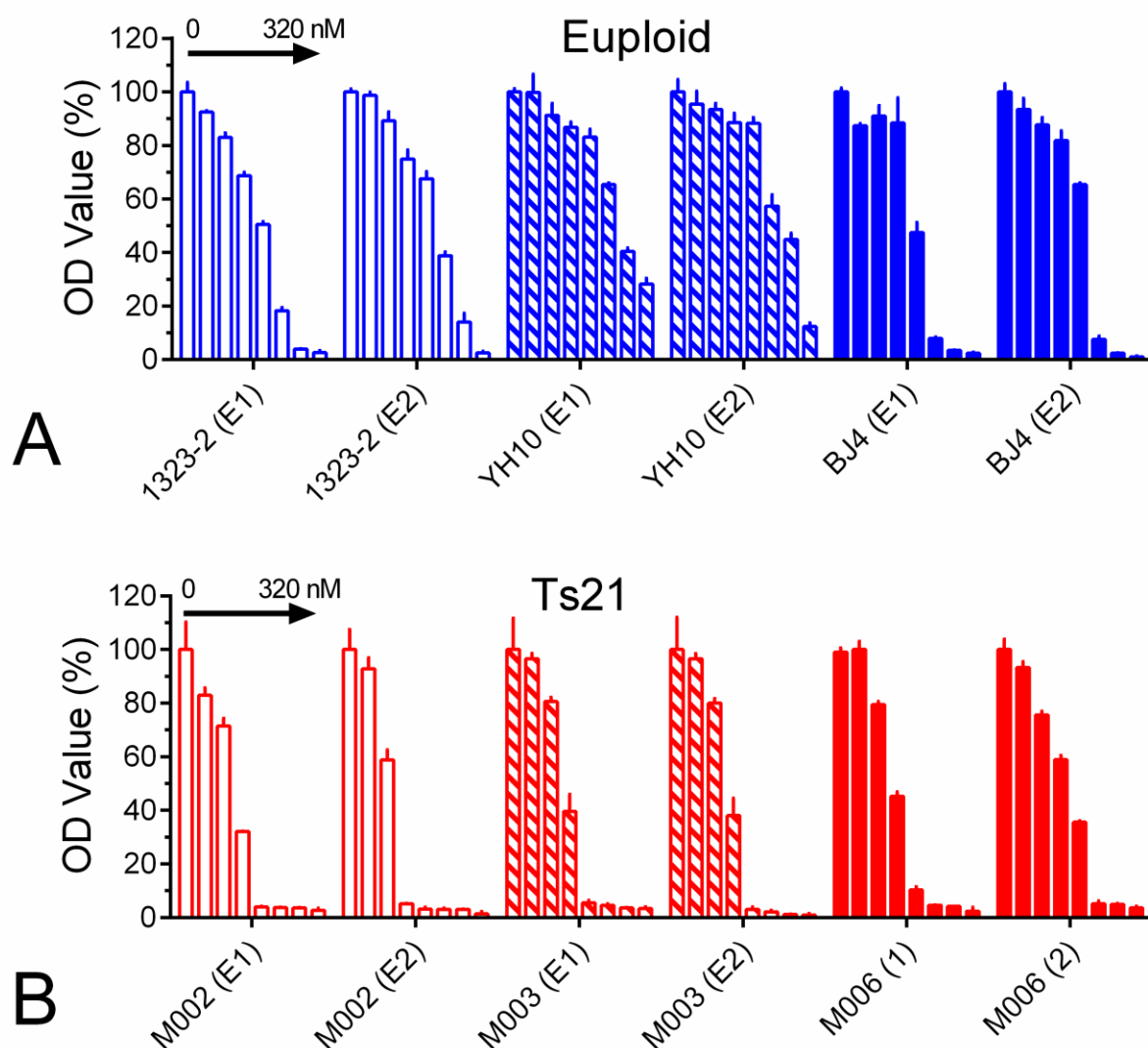**Supplemental Figure 1.**

Representative spectral karyotyping (SKY) images of chromosomes from the CWRU1002i **(A)** and CWRU1005i cell lines **(B)**. The upper panels show metaphase spread images using inverted DAPI staining (left), a spectral representation (middle), and SKY pseudocolor classification of chromosomes based on multicolor dye hybridization (right). The lower panels are the resulting karyotype tables of each cell line. The red circles highlight the trisomy of chromosome 21.

CWRU1006i-5T

CWRU1011i-3T

Supplemental Figure 2.

Representative spectral karyotyping (SKY) images of chromosomes from the CWRU1006i **(A)** and CWRU1011i cell lines **(B)**. The upper panels show metaphase spread images using inverted DAPI staining (left), a spectral representation (middle), and SKY pseudocolor classification of chromosomes based on multicolor dye hybridization (right). The lower panels are the resulting karyotype tables of each cell line. The red circles highlight the trisomy of chromosome 21.

Supplemental Figure 3.

The effect of proteotoxic compounds on T21-iPSCs. Three euploid cell lines (1323-2, YH10, BJ4) (A) and three T21-iPSC lines (CWRU1002i, -1003, -1006) (B) were treated with escalating concentrations of 17-AAG (0, 20, 40, 60, 80, 120, 160, and 320 nM). Cell survival rate of each cell lines were determined by MTT assay after 9 days, experiments were run in triplicate and repeated two times. Bar graphs represent normalized mean OD values for each triplicate experiment ± standard error. These values were used to generate the dose-response curve shown in Fig. 6A.

Supplemental Video 1.

Video corresponding to the three clusters shown in Fig. 5B, for the two time segments shown in

Fig. 5D. The frame rate was slowed down from 86.38 fps to 30 fps for clarity.