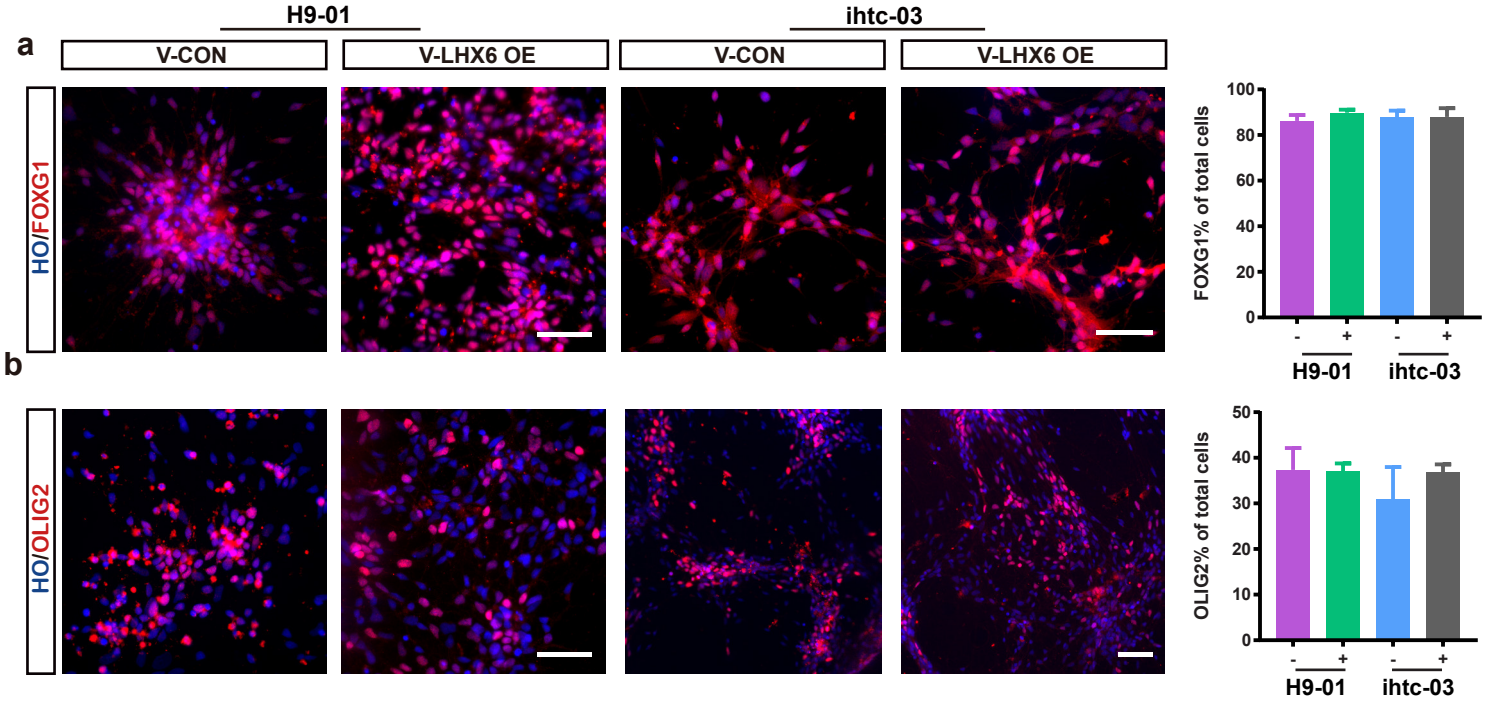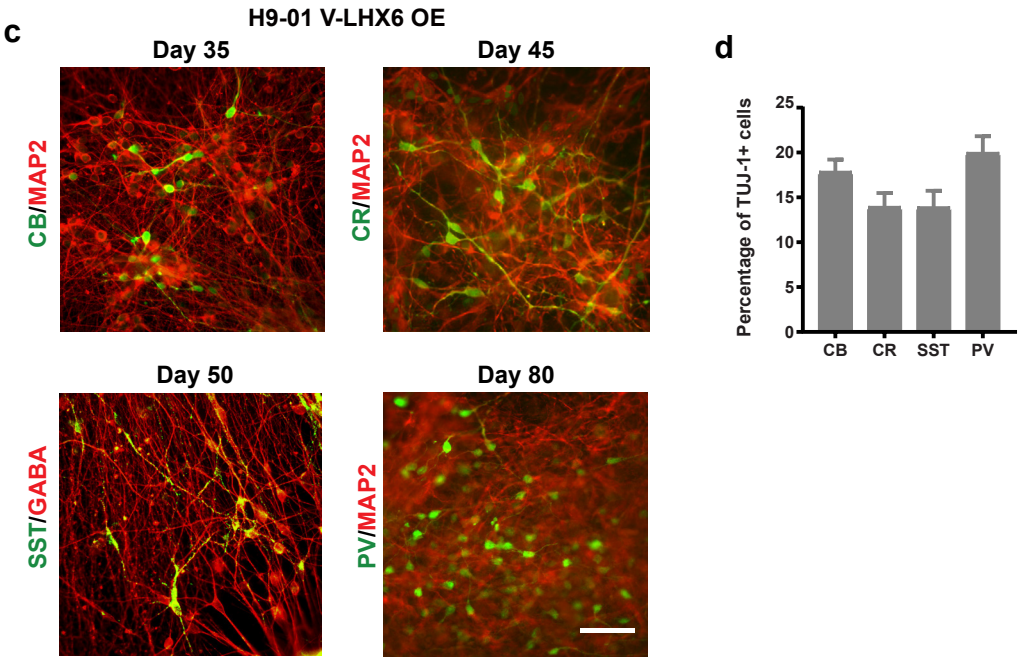Figrue 3-figure supplement 1