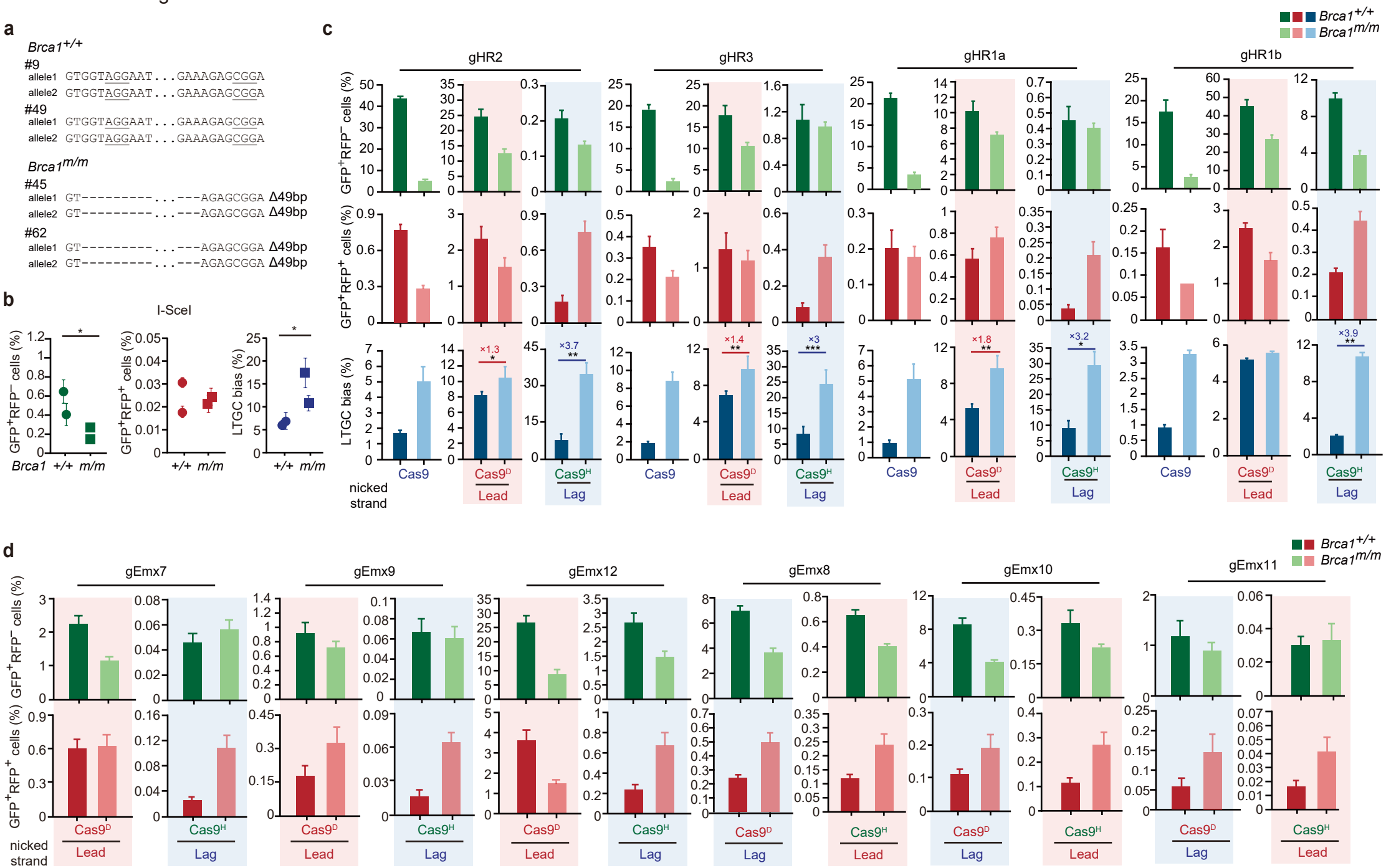Extended Data Figure 4