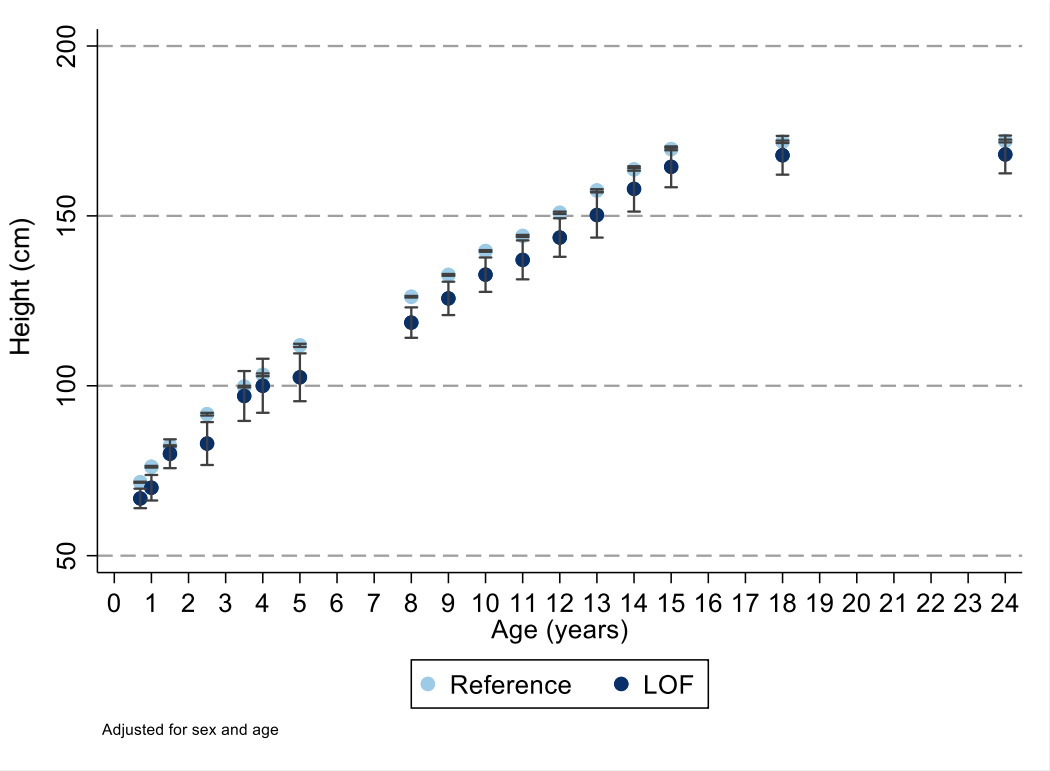
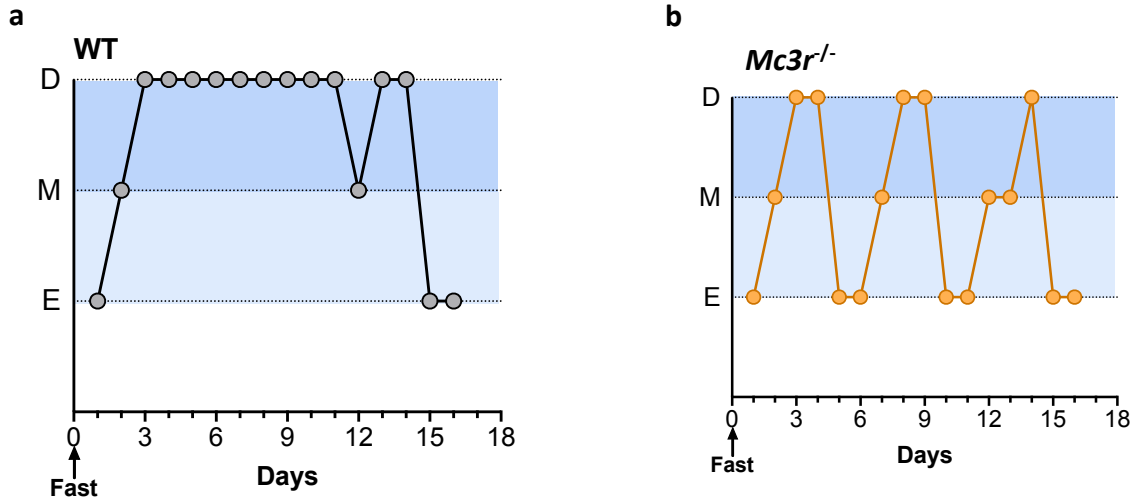
Extended data figures from accepted version of Lam et al 2021, Nature
"MC3R links nutritional state to childhood growth and the timing of puberty"
Final published article can be accessed via https://doi.org/10.1038/s41586-021-04088-9

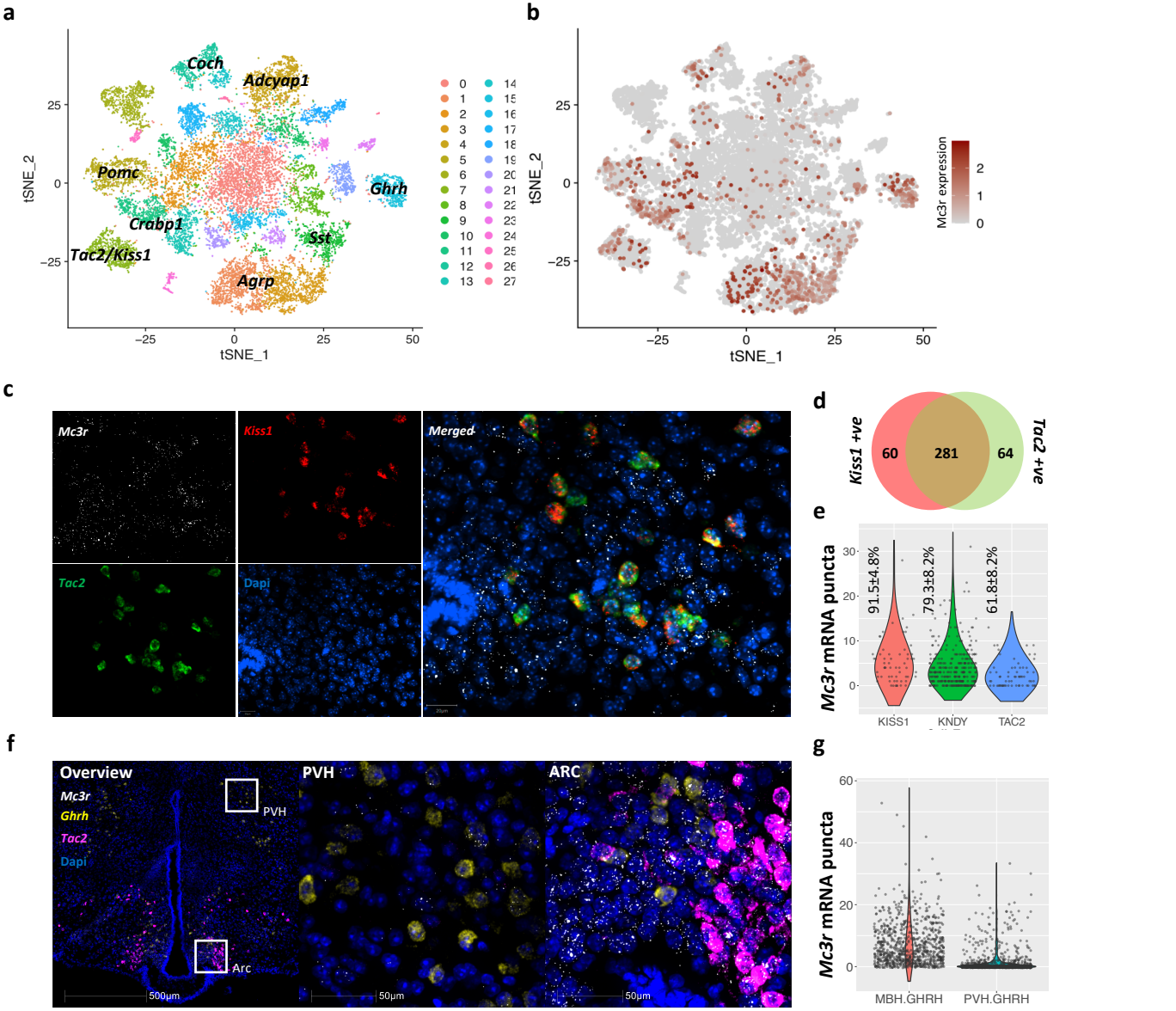


Extended Figure 1 Effect of *MC3R* Loss-of-Function (LoF) mutations on height (cm) across time
Carriers of *MC3R* LoF mutations (dark blue) had lower height throughout early life course compared to the reference group (light blue) after adjusting for sex and age. Figures only show results where the mutation group was represented by at least one individual at all time points between birth and 24 years. Error bars represent 95% confidence intervals.



Extended Data Figure 2 MC3R is essential for normal cycle length and for fasting-induced suppression of the reproductive axis.

(a & b) Representative traces of progression through the oestrous cycle in a (**a**) WT and (**b**) *Mc3r*$^{-/-}$ mouse following an overnight fast. D=Dioestrous; M=Metoestrous; E=Oestrous.



Extended Figure 3 *Mc3r* is expressed in several cell populations in the mouse hypothalamus

(a) T-SNE plot showing 28 neuronal clusters of the mouse hypothalamus from a combined dataset consisting of 18427 neurons from 4 published studies. Gene markers are available in Table S8.

(b) Mc3r is expressed in several neuronal populations (log2 normalised expression in dark red).

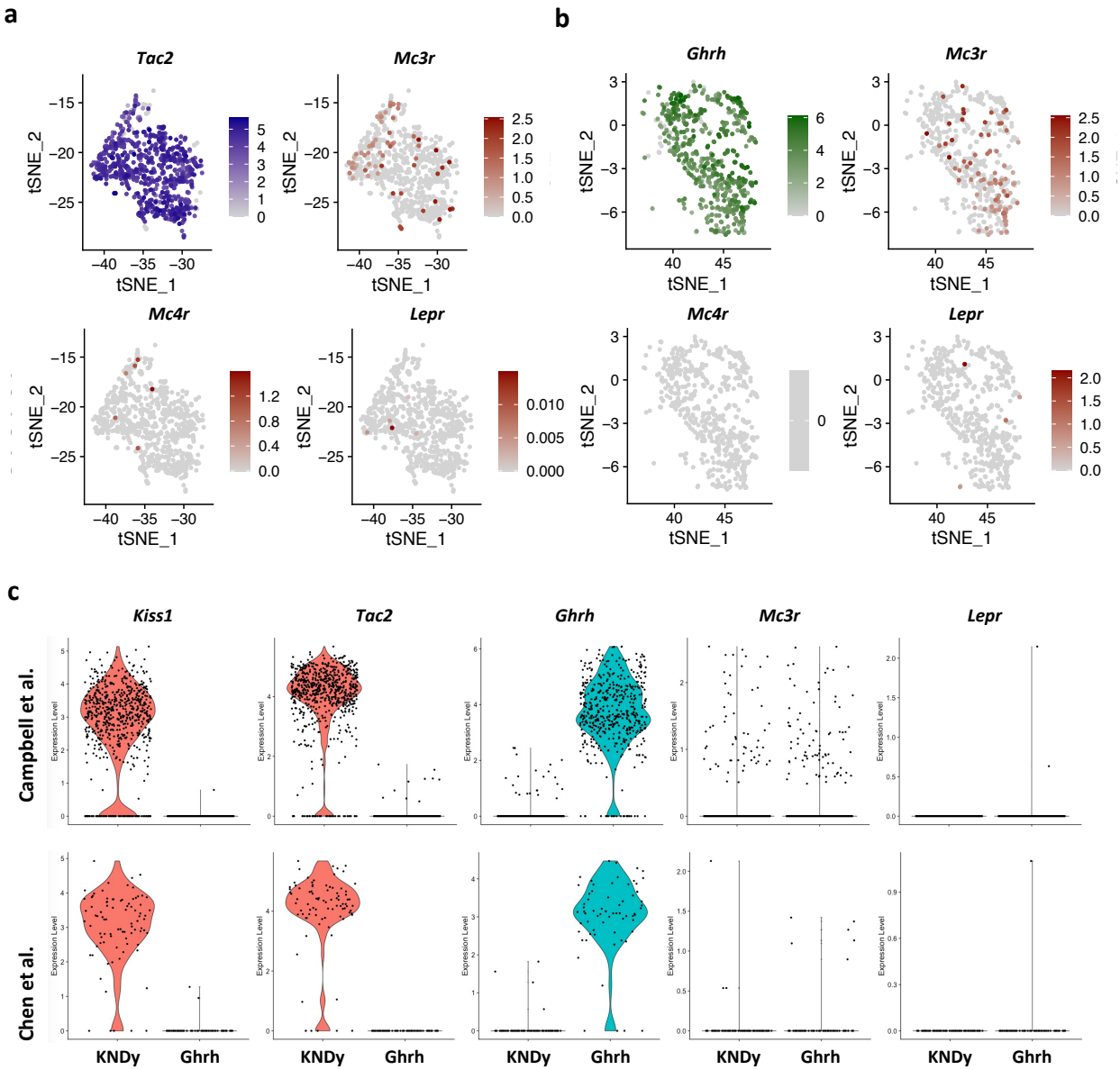
(c) Multiplexed smFISH showing the co-expression of *Mc3r* (white) *Kiss1* (red) and *Tac2* (green) in the arcuate nucleus.

(d) Venn diagram showing the number of cells expressing *Kiss1* (left), *Tac2* (right), or both (KND*y,* centre).

(e) Violin plots showing the number of Mc3r mRNA punta in *Kiss1* only, KND*y*, and *Tac2* only cells. Mean percentage of cells ± SEM with detected *Mc3r* is shown. N=3

(f) Expression of *Mc3r* (white) in *Ghrh* (yellow) positive cells in the arcuate nucleus and the dorsal paraventricular hypothalamus (PVH). Tac2 (magenta).

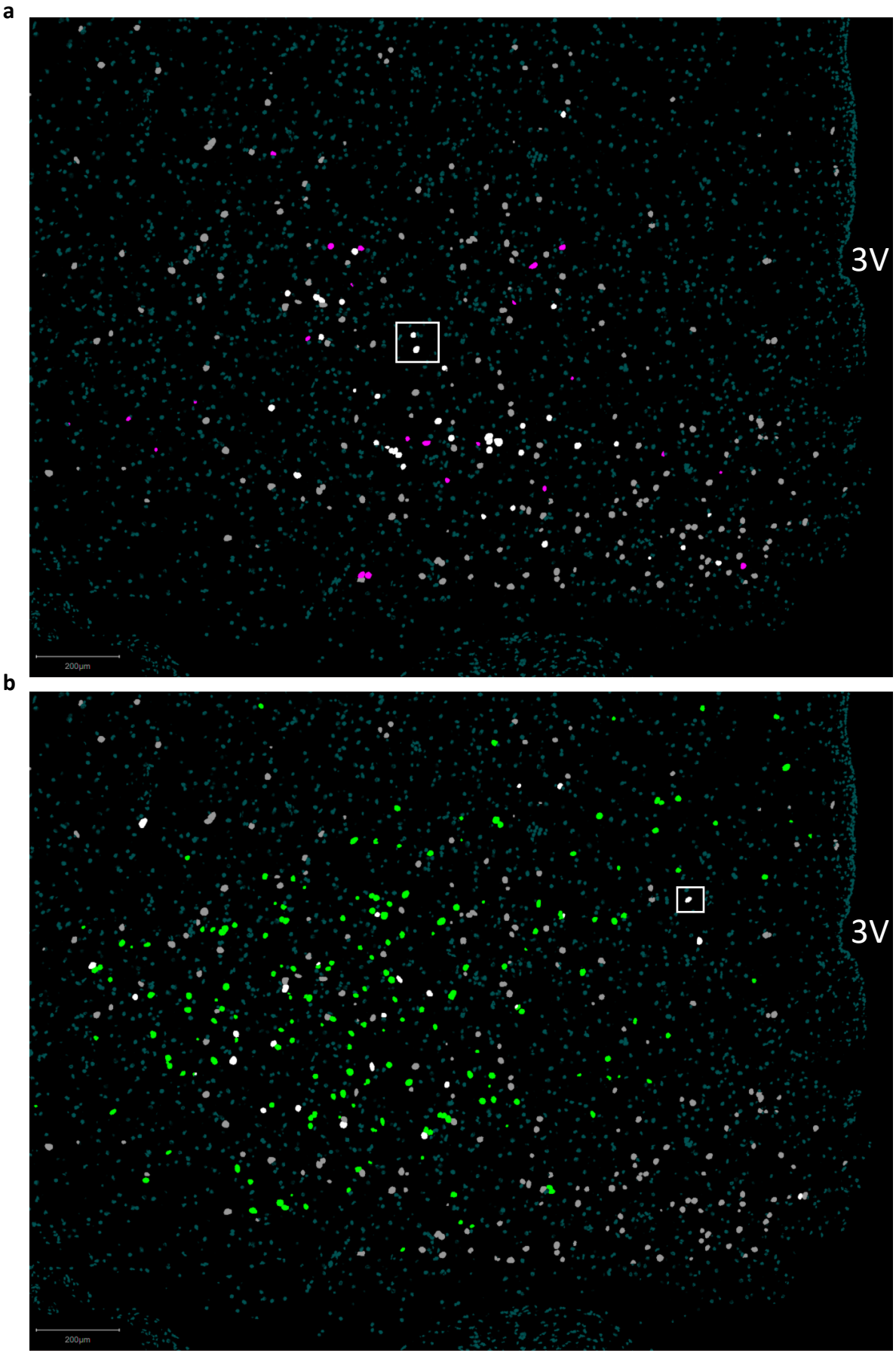
(g) Violin plots showing number of *Mc3r* mRNA puncta in GHRH neurons from the two regions.



Extended Data Figure 4 Expression of *Mc3r* and *Lepr* in KNDy and GHRH neurons

(a - b) *Mc3r* expression is more prominent compared to *Mc4r* and *Lepr* in (**a**) *Tac2* (KNDy) (cluster 7, blue) and (**b**) GHRH neurons (cluster 15, green).

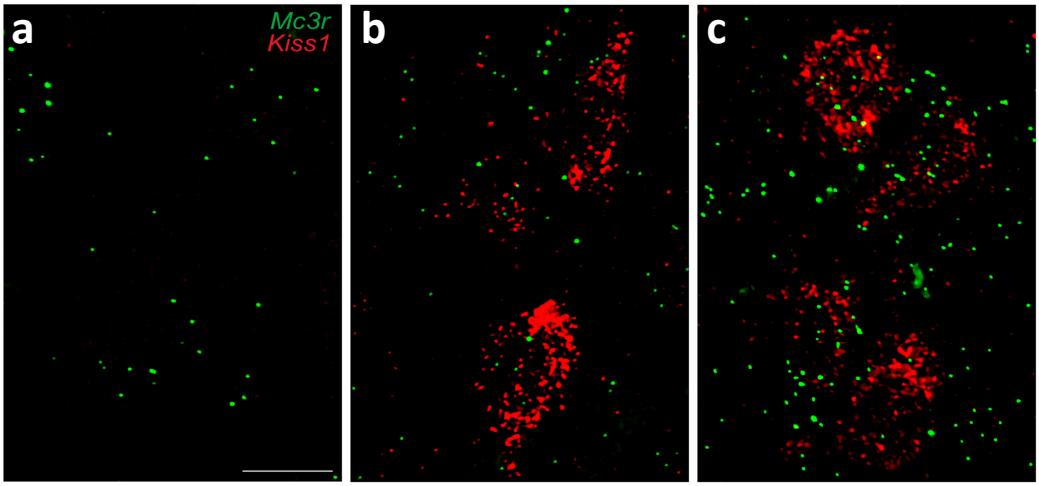
(c) Violin plots showing expression of *Kiss1, Tac2, Ghrh, Mc3r* and *Lepr* in KNDy and GHRH neurons in the Campbell[39] and the Chen[43] dataset in separate. The Lam[41] and Romanov[42] datasets are not showed due to low cell count (<10) in either clusters.



Extended Data Figure 5 Annotated overviews showing the co-expression of *MC3R, KISS1*, and *GHRH* in the human hypothalamic arcuate nucleus

(a) Co-expression of *MC3R and KISS1* was detected using smFISH: *MC3R* = grey, *KISS* = magenta and *MC3R*+*KISS1* = white. The white square marks the representative example shown in **Fig 4e** (Scale bar = 200um)

(b) Co-expression of *MC3R and GHRH* was detected using smFISH: *MC3R* = grey, *GHRH* = green and *MC3R*+*KISS1* = white. The white square marks the representative example shown in **Fig 4f** (Scale bar = 200um)



Extended Data Figure 6 Mc3r expression in kisspeptin neurons in the mouse hypothalamus at P16, P28 and P48
(**a-c**) smFISH showing the co-expression of *Mc3r and Kiss1* in the anteroventral periventricular nucleus (AVPV) at (**a**) post-natal day (P)16; (**b**) P28 and (**c**) P48: *Mc3r* = green, *Kiss1* = red (Scale bar = 20um).