Figure 3: Altered hair regenerative wave dynamics in *KRT14-NOG* mice and non-autonomous interactions with normal cycling host skin after transplantation.
(a) Control and (a') *KRT14-NOG* mice. Hair cycle domains in two different stages are shown, together with schematic domain boundaries generated by similar analysis used in supplementary Fig. S1.
(b) Measurements show both refractory and competent telogen are shortened in *KRT14-NOG* mice (green bars).
(c) Plucking/regenerative response in *KRT14-NOG* (green bars) is about 5 times faster.
(e) When a small *KRT14-NOG* skin graft was transplanted into SCID skin, hair growth (e) and duration of refractory telogen (d) were partially rescued.
(f) When a large *KRT14-NOG* skin graft (>10mm) was transplanted, it caused reduction of refractory telogen by inducing a rim of white hair from the host.
(g, h) hBMP4-soaked beads caused hair propagation wave (green arrowed curve) to go around them, creating a new telogen domain. Albumin does not have this effect. Red broken line, domain border. Scale bars: e, g, h: 1 mm.

Figure 4: Functional phases of the hair cycle.
(a) Illustration of the bulge niche microenvironment and inter-follicular dermal macroenvironment, including dermis, subcutaneous fat and adjacent follicles. Anagen stimulating (black and green) or inhibitory (red) activities are depicted with colored arrows. Follicles are in different stages: A, refractory telogen; B, competent telogen; C, propagating anagen; D, autonomous anagen follicles. Blue circle in A, intra-follicular micro-environment. Color coded similar to panel b.
(b) New functional phases (colored outer circle) mapped against classical hair cycle stages (black and white inner circle). Based on the growth-inducing ability of follicles, anagen is divided into propagating (inducing, blue) and autonomous (non-inducing, yellow) phases. Based on ability to respond to regenerative signals, telogen is divided into refractory telogen (red) and competent (green) phases.

Supplementary Methods

Choosing early versus late telogen skin

To choose early vs late telogen skin in living mice, we followed this protocol.
1) An area on the adult mouse skin where hairs appear to be growing was chosen. The use of pigmented mice makes it easier to distinguish these phases. Hairs are clipped (not plucked) near the skin surface. Anagen phase skin will contain pigment in the proximal hair follicles. This determination can be aided by observing the skin under a dissection microscope, especially when the skin is wet with saline solution to help make it appear transparent.
2) These mice are monitored daily and the day on which skin pigmentation ceases is recorded. This coincides with the anagen / catagen junction.
3) Wait for an additional 5 days to make sure skins are in early telogen. This gives us early telogen skin to work with.
4) Alternatively wait for at least 40 days (well over 4 weeks) after the anagen / catagen junction for late telogen skin to develop. This gives us late telogen skin to work with.

Scoring the plucking experiments

Hairs are plucked from the early or late telogen region. After plucking, each plucked spot is monitored daily under a dissection microscope. We can detect new anagen skin on living mice without having to biopsy or sacrifice the mice for histological specimens. We then look for changes in pigmentation since melanogenesis starts in anagen III. Pigmented hairs can be spotted under a dissection microscope before the new hair fibers reach the skin surface. Thus we are able to record non-invasively the appearance of anagen III hair follicles (when we spot black hairs under the skin surface). Approximately this corresponds to the 2nd day of new anagen. It takes another day for the new hair fiber to reach the skin surface. Thus we were also able to record non-invasively day 3 anagen follicles when the new hair filaments reach above the skin surface.

Because the changes in skin pigmentation are not easily visible, we use the appearance of new hair filaments above the skin surface as the criteria for scoring hair plucking experiments. Therefore the 9 days shown in Fig. 1f means it takes approximately 9 days to observe the appearance of day 3 anagen follicles. The extra time includes the period required for the follicle to heal and get ready to enter anagen.

Protein administration experiment

Intracutaneous administration of exogenous protein was performed as follows: Affinity chromatography Affi-gel blue gel beads were obtained from Biorad. Beads were washed in 1X PBS, followed by drying. The beads were then re-suspended in 5µl of protein solution, control (BSA 1mg/ml) or experimental (hBMP4 1mg/ml) at 4ºC for 30 min. Recombinant Human BMP4 protein was obtained from R & D Systems. Reconstitution of the protein was performed in 4mM HCl in 0.2% BSA as per the manufactures guidelines. Approximately 100 beads were introduced to the competent telogen skin of adult mice via a single puncture wound to the skin made by a 30g syringe (insulin syringe). To replenish proteins, subsequent doses of 1.5µl of protein solution were microinjected to the site of the bead implantation every 24 hours via glass micro-needle until the tissue was harvested. After we noted the anagen spreading wave pass beyond the bead implantation sites (1 week in the case of Fig. 3g, h), we collected the skin and inverted it for photography. This allows the study of the anagen wave spreading dynamics around the control and hBMP4 beads.