Micro-Injury Induces Hair Regeneration and Vitiligo Repigmentation Through Wnt/ β-Catenin Pathway

Xiaofeng Han
Beijing University of Chinese Medicine Affiliated Chongqing Traditional Chinese Medicine Hospital: Chongqing City Hospital of Traditional Chinese Medicine

Li Chang
Chongqing University

Mao Lin
Beijing University of Chinese Medicine Affiliated Chongqing Traditional Chinese Medicine Hospital: Chongqing City Hospital of Traditional Chinese Medicine

Dongwei Qi
Beijing University of Chinese Medicine Affiliated Chongqing Traditional Chinese Medicine Hospital: Chongqing City Hospital of Traditional Chinese Medicine

Yuyi Wang
Beijing University of Chinese Medicine Affiliated Chongqing Traditional Chinese Medicine Hospital: Chongqing City Hospital of Traditional Chinese Medicine

Deming Liu
Beijing University of Chinese Medicine Affiliated Chongqing Traditional Chinese Medicine Hospital: Chongqing City Hospital of Traditional Chinese Medicine

Wei Xu (davidweixucn@gmail.com)
Chongqing First People's Hospital and Chongqing Traditional Chinese Medicine Hospital
https://orcid.org/0000-0001-9195-2258

Julia Li Zhong
Chongqing University

Qingchun Diao
Beijing University of Chinese Medicine Affiliated Chongqing Traditional Chinese Medicine Hospital: Chongqing City Hospital of Traditional Chinese Medicine

---

Research

Keywords: Micro-injury, Hair regeneration, Vitiligo repigmentation, Wnt/β-catenin pathway

Posted Date: May 21st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-517912/v1

Version of Record: A version of this preprint was published at Stem Cells and Development on January 19th, 2022. See the published version at https://doi.org/10.1089/scd.2021.0276.

Abstract

Background: Extrinsic injury can evoke intrinsic stimulation subquently initiate physiological repair process. Several kinds of injury have been studied to promote hair growth and skin pigmentation. In this study, we ask if proper injury could be employed to create local stimuli subsquently to induce hair regeneration and vitiligo repigmentation.

Methods: We firstly manufactured a novel designed device to precisely control all micro-injury parameters. Then the most appropriate micro-injury extent was evaluated without over-damage to skin. The effects of micro-injury on hair regeneration and vitiligo repigmentation were examined by macroscopical observation, histological staining, gene and protein expression analysis.

Results: We discover that proper micro-injury effectively induces hair regeneration by activating the hair follicle stem cell proliferation and migration downwards to hair matrix, finally shifting the hair follicle stage from telogen into anagen. On vitiligo model mice, micro-injury also induces the hair follicle melanocyte stem cell migrate upwards to interfollicular epidermis, activate and give rise to melanocytes to repopulate vitiligo lesion. Mechanism analysis indicates that the canonical Wnt/b-catenin pathway plays a key role in the micro-injury induced regeneration process.

Conclusions: The present study demonstrates that micro-injury has great potential in inducing hair regeneration and vitiligo repigmentation, laid a foundation to develop micro-injury based treatment method in alopecia and vitiligo.

Background

Hair follicle harbors heterogenous stem cell populations contributing to hair cycle, hair color, epithelial renewal and skin color under physiological condition and/or stress condition. Extrinsic environmental stimuli, such as hair plucking[1] and mechanical stretch[2] can induce hair growth. Morever, large full thickness skin excision can induce hair negeosis in the central area of wound, a phenomenon called wound-induced HF neogenesis (WIHN) in mice[3]. These elegant studies inspire us that proper physical method could be employed to promote hair growth.

Physical stimuli, such as PUVA[4], UVB (NB-UVB)[5], CO_2 fractional laser[6], microneeding[7] were also employed in clinic to treat skin depigmentation disorders including vitiligo. In addition, clinical observation shows that vitiligo recovery usually experinces a process called perifollicular repigmentaion[8]. Recent study using lineage tracing mice exactly shows that hair follicle melanocyte stem cell (HF-McSCs) give rise to epidermal melanocyte after injury or UVB treatment[9]. All these studies suggest that hair follicle serve as a cell reservoir for fuctional interfollicular epidermal melanocytes upon injuries.

Wnt signal plays a vital role both in hair regeneration and vitiligo repigmentation. The canonical Wnt signaling pathway hallmarked by the event of cytosolic β-catenin stabilization and its subsequent

translocation to the cell nucleus, where it interacts with LEF/TCF transcription factors to activate downstream gene transcription[10], including the key melanogenesis genes Mitf, TRP1, TRP2 (also known as DCT) and tyrosinase (TYR)[11, 12].

However, what extent of proper injury can induce local reaction and whether the injury stimuli can induce hair growth and/or skin pigmentation need more exploration. In this study, by a fine customer-made instrument we discover that proper injury stimulation effect both on hair regeneration and vitiligo repigmentation through injury induced Wnt/β-catenin pathway.

Methods And Materials

Customer-made micro-injury instrument

To standardize the micro-injury, we designed and made a fine instrument to control the depth, density and temperuture of the injury (Fig. S1A). The density was achieved by a disposable multi-needle head (Fig. S1B), in the present study we set at 0, 10, 20, 30, 40, 50, 60 needles/cm^2, which create the corresponding micro-injuries/cm^2. The depth was controlled by a fastener on the head, in the present study was set at 2 mm, which approximately reach dermis. The temperuture is controlled by an electromagnetic heating unit to make the needles at 500℃ for easily acupucturing into skin. All parameters were set by the instrument instead of controlling by manual operation.

Animals

C57BL/6 mice were obtained and feed at Laboratory Animal Center of the Third Military Medical University, Chongqing, China. Dct-LacZ transgenic mice were generated by Prof. Ian Jackson[13], then were backcrossed with C57BL/6J. and were kindly provided by Prof. Haiying Guo [14]. All animal procedures were performed under the ethical guidelines of Laboratory Animal Welfare and Ethics Committee Of the Third Military Medical University.

Vitiligo mouse model

Adult C57BL/6 mice tail were employed for vitiligo model because melanocytes resist in tail epidermis. We established vitiligo model as previously[15]. Briefly, 50 μg TRP2-180 (Anaspec, Fremont, CA, USA), 5 μg LPS (Invivogen, San Diego, CA, USA) and 5 μg ODN 1826 (invivogen, San Diego, CA, USA) were mixed for immune-induced depigmentation. Seven week-old male C57BL/6 mice were immunized subcutaneously at the hind footpad once a week for 2 weeks, followed by immunizing intradermally in the tail dermis once a week for 2 weeks. Control mice were immunized with PBS. Four to 5 weeks after the last immunization, immunized mice should develop a depigmented skin lesion around the tail injection site.

Micro-injury, XAV939 injection and sample collection

For hair regeneration, 7 week-old male C57BL/6 mice whose hair cycle enter in telogen were employed for micro-injury. After anaesthesia and hair cut, mice were made micro-injuries distributedly on their dorsal

skin twice a week at different dose or different time. Self-control (sham injury) was made on neighber area of each dorsal skin. Hair growth was monitored by taking pictures before each times of injury. Skin samples from dose group were harvested for histological examination at the end of 3 weeks. Skin samples from time group were harvested 2 days after the last injury.

For vitiligo repigmentation, established vitiligo mice were employed for micro-injury once a week. We chose 30 micro-injuries/cm^2 because this dose could make greatest injury stimulaiton without obvious skin damage. Tail skin color was monitored by taking pictures before each times of injury. Skin samples were harvested for histological examination, gene and protein analysis at indicated timepoint.

For blocking the Wnt/β-catenin pathway, mice were injected i.p. with 100μl XAV939 (1mg/ml, MCE, Shanghai, China) every day until harvesting samples. A volume of 100μl 10% DMSO/90% 0.9% NaCl, the solvent for XAV-939, were injected i.p. as control.

qPCR

Primer Pairs Used for Quantitative Real-Time PCR are listed in Table 1.

Table 1
Primer Pairs Used for Quantitative Real-Time PCR

Target gene	Primer	Sequence (5'-3')	PCR product size (bp)
GapdH	Forward	GGTTGTCTCCTGCGACTTCA	220
	Reverse	TAGGGCCTCTCTTGCTCAGT	
TRP1	Forward	TTCATGGTACTGGTGAGCAGC	200
	Reverse	ACTCTCGTGGAAACTGAGCC	
TRP2	Forward	CCTGAATGGGACCAATGCCT	125
	Reverse	AGGCATCTGTGGAAGGGTTG	
TYR	Forward	ATCGGCCAACGATCCCATTT	116
	Reverse	TAGGTGCATTGGCTTCTGGG	
MITF_M	Forward	CTCGGGATGCCTTGTTTATG	101
	Reverse	GAGACACCGCAGACCACTTAG	
Wnt10b	Forward	TTCTCTCGGGATTTCTTGGATTC	118
	Reverse	TGCACTTCCGCTTCAGGTTTTC	
β-catenin	Forward	GGGTGCTATTCCACGACT	127
	Reverse	CCCTTCTACTATCTCCTCCAT	
LEF1	Forward	CTTTGGTTAACGAGTCCGAAA	62
	Reverse	GGCTTGTCTGACCACCTCA	

Western blotting

Western blotting was performed as follows: the tissue lysates were separated on 12% SDS-polyacrylamide gels and transferred onto polyvinylidene fluoride membranes (Bio-Rad). Antibodies including anti TRP1 (Santa Cruz, sc-25543), TRP2 (Santa Cruz, sc-25544), Mitf_M (Abcam, ab49387), Wnt10b (Zen-bioscience, 220359), β-catenin (Cell Signaling Technology, 8480), LEF1 (Cell Signaling Technology, 2230S) were incubated with the membranes. The Western blot results were further analyzed using a Bio-Rad ChemiDoc™ XRS$^+$ system.

H.E. Staining, Fontana-Masson staining, LacZ staining and immunofluorescence staining

H.E. staining was performed on paraffin-embedded sections for examing hair growth. Fontana-Masson staining was employed to display the amount and distribution of melanin. LacZ staining was employed to trace the cells expressing beta galactosidase in skin. Skin samples from Dct-LacZ mice were embed in

OCT on dry ice. After frozen section, slides were fixed in fix solution (2% formaldehyde, 0.25% glutaraldehyde, 2 mM $MgCl_2$ in PBS (pH 7.4)) for 20 min on ice. The fixed slides were rainsed in detergent solution (2 mM $MgCl_2$, 0.01% NP-40 in PBS) for 10 min on ice followed by staining in 5-bromo-4-chloro-3-indolyl-B-D-galactoside (X-gal) (Invitrogen, CA) solution at 37℃ for 3 h in dark. The stained tissues were postfixed with 10% formalin solution and were counterstained with eosin for 3 min. Immunofluorescence staining was performed with anti K15 (Abcam, ab52816), PCNA (Cell Signaling Technology, 2586), β-catenin (Sigma C7207), β-galactosidase (Abcam, ab9361) followed by secondary antibodies conjugated to Alexa-488 or Alexa-546.

Statistical analysis

Data were presented as the mean ± S.D. Statistical analyses were performed using GraphPad Prism version 5.0 (GraphPad Software, La Jolla, CA, USA). A two-tailed Student's t-test was performed to calculate statistical significance for differences between two groups. In all cases, $P \leq 0.05$ was considered statistically significant.

Results

Micro-injury induces hair regeneration

For choosing an optimal injury density, 6 groups of mice were created with 10, 20, 30, 40, 50, 60 micro-injuries/cm^2 on their dorsal skin twice a week for 3 weeks. Comapred to self-control (sham injury, upper circles), micro-injury (lower circles) can induce hair growth from 10–30 micro-injuries/cm^2 on a dose-dependent manner. While 40–60 micro-injuries/cm^2 can not induce hair growth effectively, probably due to the over-damage to hair follicles (Fig. 1A). Histology results show that hair follicles entered anagen in 30 micro-injuries/cm^2 group while the hair follicles with sham-injury remain in telogen, histological analysis also indicates the over-damage of skin in 60 micro-injuries/cm^2 group, which could explain the delay of hair growth (Fig. 1B). Therefore we next chose the optimal 30 micro-injuries/cm^2 to study the times effect of micro-injury on hair regeneration. Macroscopical observation show that micro-injury promotes hair growth with micro-injury times increasing (Fig. 1C). H.E. staining show that micro-injuries can induce hair cycle transition from telogen to anagen in a time-dependent manner (Fig. 1D). Immunofluorescence show that micro-injuries induce $K15^+$ hair follicle stem cell proliferation (Fig. 1E). These results demonstrate that micro-injury induces hair regeneration by shifting the hair follicle stage from telogen into anagen.

Micro-injury induces vitiligo repigmentation

We firstly established a vitiligo model on mouse tail skin. TRP2-180 peptide immunization readily induced skin depigmentation (Fig. 2A). Compared to the model group which depatched skin remain white after 2 months, micro-injury grandually induces repigmentation during 2 months, indicate the injury stimulation is effective on vitiligo treatment (Fig. 2A). Fontana-Masson staining also verify that melanocytes

regenerate increasely in vitiligo lesion (Fig. 2B). LacZ staining in model group locates the Dct-LacZ$^+$ hair follicle melanocyte stem cells (HF-McSCs) in hair bulge (Fig. 2C). While after micro-injury treatment, LacZ$^+$ HF-McSCs migrate into epidermis, indicating that HF-McSCs response for perifollicular repigmentation in vitiligo lesion (Fig. 2C). Gene expression analysis show that all melanogenesis gene expression level increase with micro-injury (Fig. 2D). Western blotting also show that pigment-related proteins increase significantly (Fig. 2E).

Micro-injury induces hair regeneration and vitiligo repigmentation through Wnt/β-catenin pathway

We investigated the micro-injury effect on Wnt/β-catenin pathway. Gene and protein expression analysis show that Wnt 10b, β-catenin, Lef-1 increase significantly with injury time (Fig. 3A, B). Immunofluorescence staining of β-catenin shows a nuclear accumulation in the hair matrix (Fig. 3C), while duol immunofluorescence staining shows nuclear β-catenin accumulation in the migrated β-gal$^+$ melanocytes within the vitiligo lesion epidermis unpon micro-injury (Fig. 3D). Blocking the Wnt signal by XAV939 delay the hair regeneration (Fig. 4A) and vitiligo repigmentation (Fig. 4B). This effect is based on reduced β-catenin and Lef-1 expression (Fig. 4C). Thus the effect of micro-injury on hair regeneration and vitiligo repigmentation work through the Wnt/β-catenin pathway. Together, these data demonstrate that micro-injury induces hair regeneration and vitiligo repigmentation through Wnt/β-catenin pathway (Fig. 4D).

Discussion

Studies have pointed out the importance of using injury-induced effect in promoting hair growth. The outstanding one of them is the study on hair plucking-induced hair regeneration[1], which shows the hair plucking-created minor injury lead to a larger scale hair regeneration by activating the neighberhood hair follicle stem cells. The other representative one is the wound-induced hair neogenesis (WIHN) study[3], showing us a large injury enviroment (> 1 cm^2 on mouse skin) simulates the embryonic development path thus forms new hair at the centre of the wound. Absolutely, these studies showed us a injury-based therapy potential on hair regrowth even regeneration. However, these studies are concept-verified and are currently difficult to apply in clinic treatment, for hair plucking is unacceptable for patients who are anxious about hair lossing and thirst for hair regrowth, as well as a large tramua is difficult to achieve in clinic practice. In this study, we used a customer-made heat micro-needle instrument to create standard minor injuries on skin and verified it’s effective application in promting hair growth, establishing it’s potential application in treating hair loss disorders.

As a classical type of depigmentation skin disorders, vitiligo treatment is still under developing. Usually clinicials treat the disorder from two steps, delay and hold the broadening of the white patch in progressive stage followed by re-establishing pigmentation during stable stage. Among several sources for the re-populate melanocytes, hair follicle represents a primary cell reservoir indicating by a familiar

recovery process called hair follicle island[8], which showing a hair-initiated pigmentation “island” in white patch “ocean”. However, current first-line method to treat vitiligo are time-consumered, thus needs to develop additional methods. Injury has showed potential in inducing skin pigmentation such as microneeding alone[7] or combined with phototherapy[16, 17], CO_2 fractional laser[6]. In this study, we showed an effective melanocytes regeneration induced by creating micro-injury on vitiligo leision, validating the conception that bulge McSCs migrate from the hair follicle to the epidermis after wounding and providing a scientific basis for developing alternative method beyond current therapy methods.

Further studies, informed by the work reported here, are needed to complete our understanding of how the extrinsic environmental micro-injury evoke the intrinsic Wnt ligands subseqently leading to the initiation of the regeneration process, and what kind of suitable regimens for micro-injury treatment of AA and vitiligo in clinic treatments.

Conclusions

In conclusion, the present study designed and manufactured a precisely controlled instrument to create micro-injury on skin and tested their effect on hair regeneration and vitiligo repigmentation. Resluts demonstrate that proper micro-injury effectively mobilizated the HF-SC migrate downwards to hair matrix to contribute to hair growth, as well as the HF-McSCs migrate upwards to interfollicular epidermis to repopulate vitiligo melanocytes (Fig. 4C). Mechanism analysis show that Wnt/β-catenin pathway plays a key role in the micro-injury induced process. This study laid a foundation to develop micro-injury based treatment method in alopecia and vitiligo.

Abbreviations

Wnt: Wingless-type mouse mammary tumor virus integration site; HF-McSCs: hair follicle melanocyte stem cells; HF-SCs: hair follicle stem cells; qPCR: quantitative real-time PCR.

Declarations

Acknowledgements

We thank Dong Li at Chongqing Medical University for helping design and manufacture the micro-injury instrument.

Funding

This work was supported by the National Natural Science Foundation of China (81503588) and the Natural Science Foundation of Chongqing (cstc2018jcyjAX0759, cstc2015jcyjA10113, 2020ZY013906, jxyn2019-1-1, CQSZYY2020011).

Availability of data and materials

All data generated in this study are included in the manuscript.

Authors’ contributions

WX, JLZ, QD designed the conceptual idea for this study. XH and LC performed most of the experiments and they contributed equally to the paper. ML, DQ, YW, DL helped perform part of experiments and analysis. All authors read and approved the final manuscript.

Authors’ information

XH, ML, DQ, YW, DL, WX, QD work in Department of Dermatology, Chongqing First People's Hospital and Chongqing Traditional Chinese Medicine Hospital. JLZ works in Bioengineering college and Life Science College, Chongqing University. LC was a joint-trainee and got her master degree.

Ethics approval and consent to participate

Ethical approval to conduct the study was obtained from the Laboratory Animal Welfare and Ethics Committee of the Third Military Medical University.

Consent for publication

All the authors give their consent for publication.

Competing interests

The authors declare that they have no competing interests.

References

1. CHEN CC, WANG L, PLIKUS M V, et al. Organ-level quorum sensing directs regeneration in hair stem cell populations [J]. Cell. 2015;161(2):277–90.
2. CHU S Y, CHOU C H, HUANG HD, et al. Mechanical stretch induces hair regeneration through the alternative activation of macrophages [J]. Nature communications. 2019;10(1):1524.
3. ITO M, YANG Z, ANDL T, et al. Wnt-dependent de novo hair follicle regeneration in adult mouse skin after wounding [J]. Nature. 2007;447(7142):316–20.

4. WU CS, LAN C C, WANG L F, et al. Effects of psoralen plus ultraviolet A irradiation on cultured epidermal cells in vitro and patients with vitiligo in vivo [J]. Br J Dermatol. 2007;156(1):122–9.
5. GOLDSTEIN N B, KOSTER M I, HOAGLIN L G, et al. Narrow Band Ultraviolet B Treatment for Human Vitiligo Is Associated with Proliferation, Migration, and Differentiation of Melanocyte Precursors [J]. Journal of Investigative Dermatology. 2015;135(8):2068–76.
6. HU Y, QI X. HU Y, et al. Effects of CO2 fractional laser therapy on peripheral blood cytokines in patients with vitiligo [J]. Dermatol Ther. 2019;32(4):e12992.
7. ANDRADE LIMA E V, AANDRADE LIMA M M D, MIOT HA. Induction of Pigmentation Through Microneedling in Stable Localized Vitiligo Patients [J]. Dermatologic surgery: official publication for American Society for Dermatologic Surgery [et al]; 2019.
8. CUI J, SHEN L Y, WANG GC. Role of hair follicles in the repigmentation of vitiligo [J]. J Invest Dermatol. 1991;97(3):410–6.
9. CHOU W C, TAKEO M, RABBANI P, et al. Direct migration of follicular melanocyte stem cells to the epidermis after wounding or UVB irradiation is dependent on Mc1r signaling [J]. Nature medicine. 2013;19(7):924–9.
10. BARKER N. The canonical Wnt/beta-catenin signalling pathway [J]. Methods in molecular biology. (Clifton NJ). 2008;468:5–15.
11. WANG X, LIU Y, CHEN H, et al. LEF-1 Regulates Tyrosinase Gene Transcription In Vitro [J]. PloS one. 2015;10(11):e0143142.
12. TAKEDA K, YASUMOTO K, TAKADA R, et al. Induction of melanocyte-specific microphthalmia-associated transcription factor by Wnt-3a [J]. J Biol Chem. 2000;275(19):14013–6.
13. MACKENZIE M A, JORDAN S A, BUDD P S, et al. Activation of the receptor tyrosine kinase Kit is required for the proliferation of melanoblasts in the mouse embryo [J]. Developmental biology. 1997;192(1):99–107.
14. GUO H, YANG K, DENG F, et al. Wnt3a promotes melanin synthesis of mouse hair follicle melanocytes [J]. Biochem Biophys Res Commun. 2012;420(4):799–804.
15. CHO Y H YOUS, BYUN JS, et al. Melanocyte-specific CD8 + T cells are associated with epidermal depigmentation in a novel mouse model of vitiligo [J]. Clin Exp Immunol. 2013;174(1):38–44.
16. EL-ZEFTAWY A A A. Comparative Clinical and Histological Study of Narrow Band UVB Phototherapy Versus Combined Narrow Band UVB Phototherapy and Microneedling in Treatment of Vitiligo [J]. Medical Journal of Cairo University. 2019;87(3):9.
17. ELNOKALY R M, SAYEDAHMED O M E, MOHAMED H A. K. Comparative Study Between the Efficacy of Microneedling Combined with Trichloroacetic Acid Versus Microneedling with Tacrolimus in the Treatment of Stable Vitiligo [J]. International Journal of Medical Arts, 2021, 1188–94.

Figures

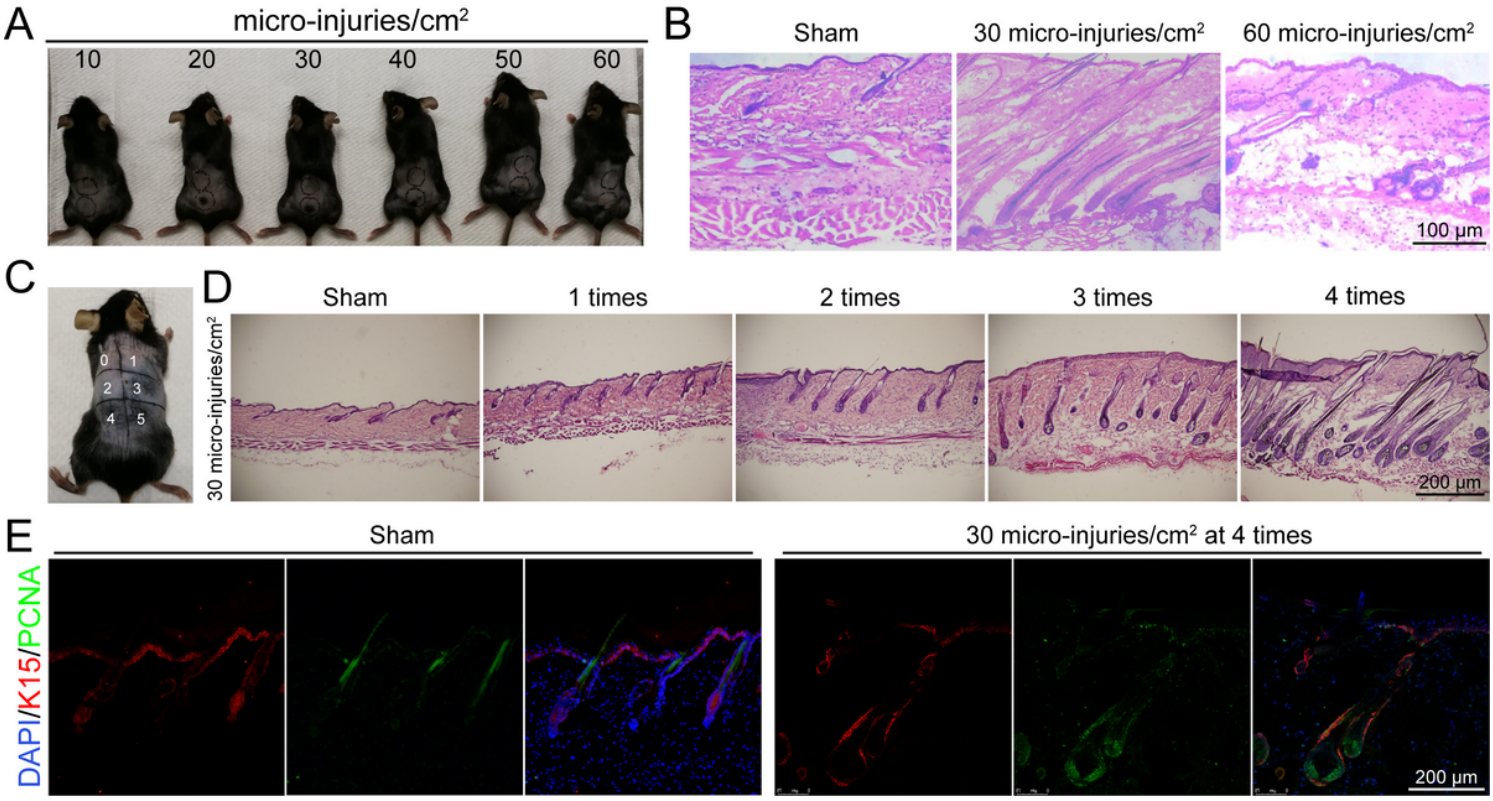

Figure 1

Micro-injury induces hair regeneration. (A) Repensentive images show mice treated with sham injury (upper circles) and 10-60 micro-injuries (lower circles) in 1 cm2 area on their dorsal skin after 6 times' injury. (B) H.E. staining show mice treated with sham injury, 30 micro-injuries/cm2, 60 micro-injuries/cm2 after 6 times' injury. Repensentive images (C) and H.E. staining (D) show mice treated with different times at 30 micro-injuries/cm2. (E) Dual immunostaining for K15 and PCNA revealed that K15+ hair follicle stem cells began to proliferate upon micro-injury.

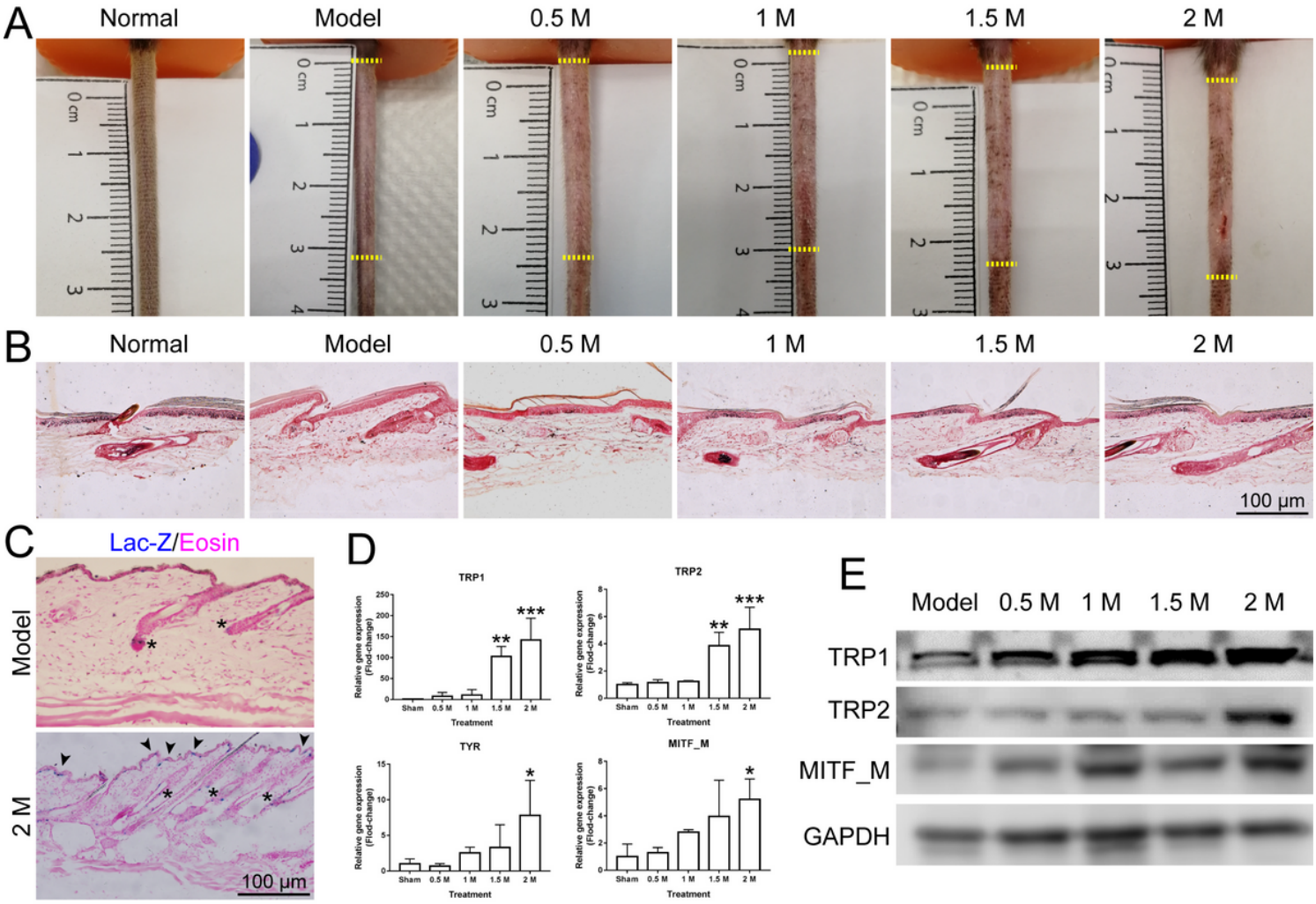

Figure 2

Micro-injury induces vitiligo repigmentation. (A) Repensentive images show vitiligo mice treated with micro-injuries at differnent times. Yellow dashed lines show the boundary of vitiligo lesion and health skin. (B) Fontana-Masson staining shows the amount and distribution of melanin in vitiligo lesion. (C) LacZ staining traces DCT+ hair follicle melanocyte stem cells (HF-McSCs) in hair bulge (marked by *) and their offspring cells in epidermal vitiligo lesion (marked by arrowheads). (D) qRT-PCR analysis of melanogensis gene expression in vitiligo lesion. *p<0.05, ** p <0.01. n=6 for each group. Compared with the sham group. (E) Western blotting test of pigment-related proteins in vitiligo lesion.

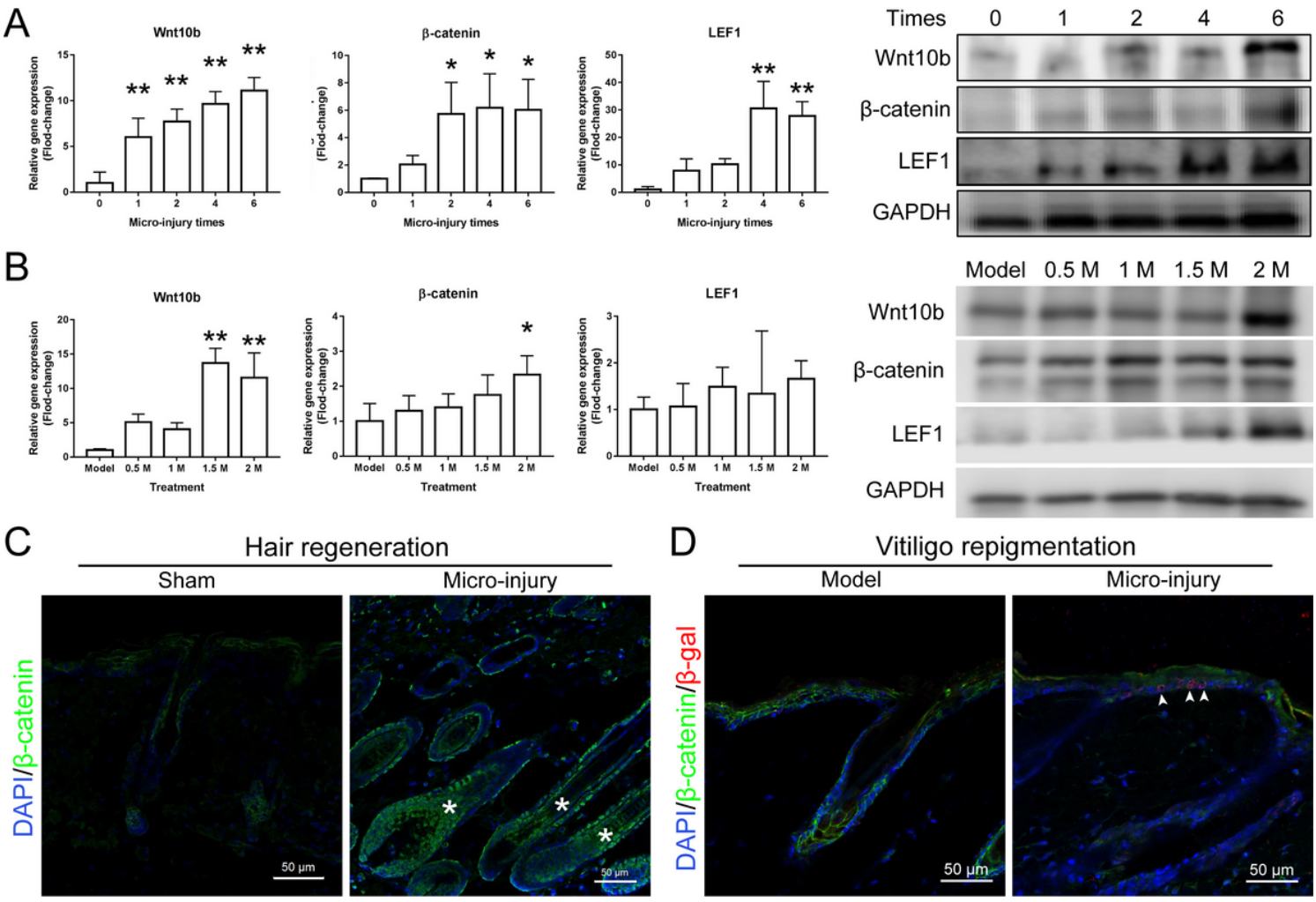

Figure 3

Wnt/β-catenin signal pathway activation in the process of micro-injury induced hair regeneration and vitiligo repigmentation. qRT-PCR and Western blotting analysis of Wnt/β-catenin pathway key factors in injured back skin (A) and vitiligo lesion (B). *p<0.05, ** p <0.01, *** p <0.001. n=6 for each group. Compared with the sham group. (C) Immunostaining shows β-catenin translocates into cell nuclear in the hair matrix (indicated by *) in micro-injured back skin. (D) Duol immunostaining shows β-catenin accumulation in the migrated β-gal+ melanocytes (indicated by arrowheads) within micro-injured vitiligo lesion epidermis.

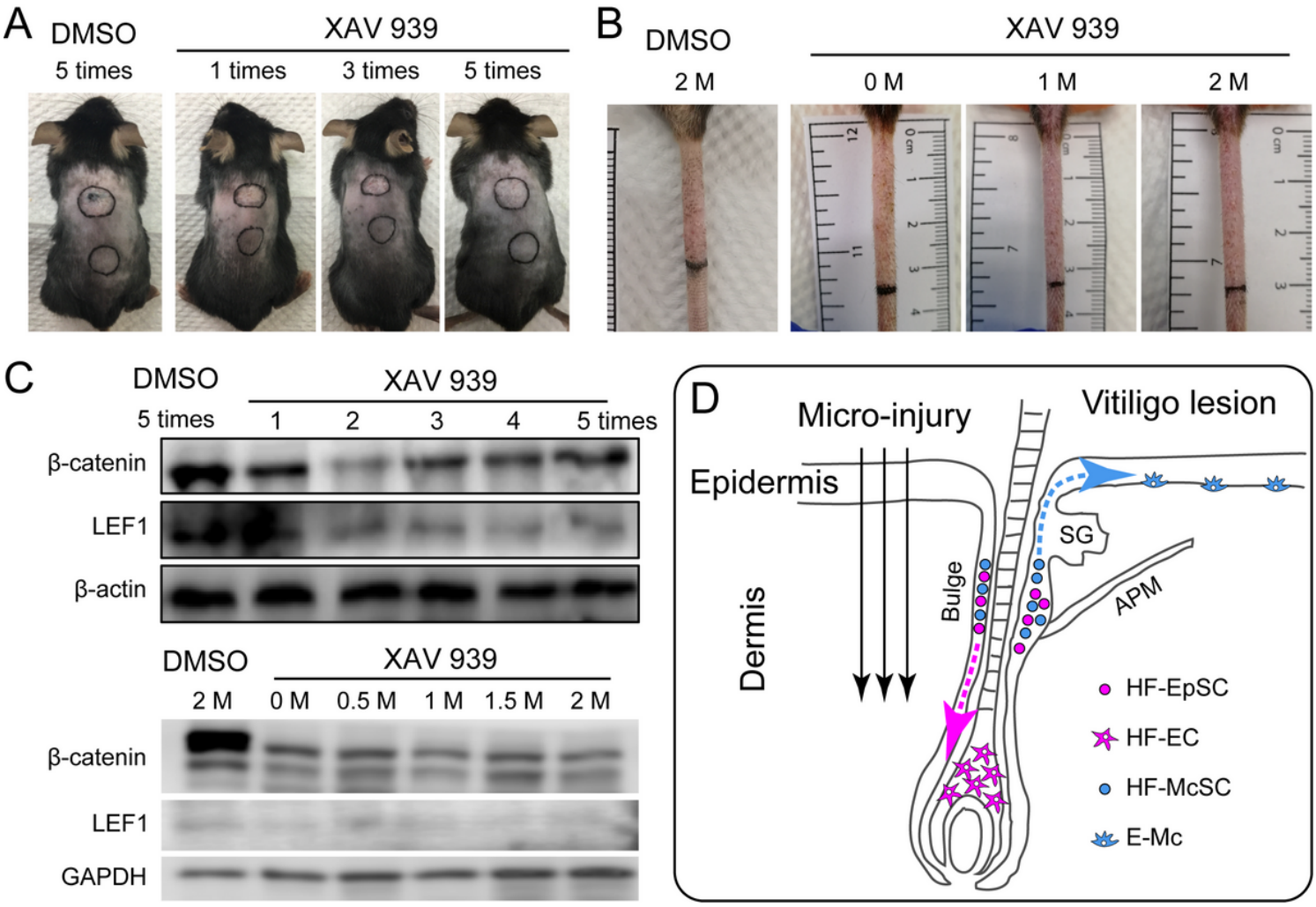

Figure 4

Blocking the Wnt signal delay micro-injury induced hair regeneration and vitiligo repigmentation. Repensentive images show hair growth (A, upper circles) and vitiligo repigmentation (B) delay in micro-injuried mice compared between XAV939 treatment and DMSO control. (C) Western blotting show β-catenin and Lef-1 expression inhibition in XAV939 mice compared to DMSO control in hair regenerated (upper) and vitiligo repigmentation (lower) mice. (D) Schematic mechanism of hair follicle epithelial stem cell and melanocyte stem cell give rise to hair regeneration and vitiligo repigmentation upon micro-injury. SG,sebaceous gland; APM, arrector pili muscle; HF-EpSC, hair follicle epithelial stem cell; HF-EC, hair follicle epithelial cell; HF-McSC, hair follicle melanocyte stem cell; E-Mc, epidermal melanocyte.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Fig.S1.tif