American Journal of Biology and Natural Sciences
https://biojournals.us/index.php/AJBNS
ISSN: 2997-7185

Modulating the Wnt/B-Catenin Pathway to Enhance Wool Fiber Fineness in Sheep: Subject Review

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Received: 2024, 15, May
Accepted: 2025, 21, Jun
Published: 2025, 08, Jul

Annotation: This review summarises the important role of the Wnt/β-catenin signal pathway in the development of wool fineness and quality traits in sheep. Here, we combined these results and performed multi-omics analysis with machine-learning algorithms, upon a systematic review of >120 peer-reviewed studies (2010–2024) and unpublished field surveys. There are reports on SNPs of CTNNB1 and LRP6, as well as CRISPR/Cas9-mediated knock-outs of FGF5, extending Anagen, increasing density of secondary follicles, reducing average fiber diameter by 1–2 μm and increase of yield can reach by 18 %. Supplementary feeding of organic zinc and selenium together with PPD II almost doubled nuclear β-catenin activity; however, chronic heat stress shortened Anagen and increased fiber thickness. Oral pulse dosing of GSK-3β inhibitor CHIR-990218 increased Comfort Factor by 6 points and decreased fiber diameter by approximately 1 μm without systemic toxicity, whereas recombinant

DKK1 served as an effective counter-screen for dose optimization. Economic modelling suggests that a 1-micron reduction in fibre diameter increases the price for scoured wool by 8–10 %, thus enabling breeding and/or pharmacological intervention to be recouped over two shearings in a flock of 1 000 ewes. Current barriers include the risks of off-target editing, fragmented regulatory landscape, and consumer acceptance of transgenic animals. We propose therefore a stepping-stone to our survival: (i) combining selection for specific Wnt markers with micro-dosing of GSK-3β inhibitors and early-warning omics dashboards, currently sighted alongside a single ethical–regulatory guideline as a roadmap for economicisation and environmental stewardship of the Merino wool industry.

Keywords: Wnt/β-catenin, Wool follicles, Gene editing (CRISPR), environmental management.

Introduction

Wool is one of the most valuable animal fibres in the high-end textile industry. Although its annual output of greasy wool is only about 1.9 million tonnes—less than 2 % of the total global fibre market—its unique physical properties (high elasticity, excellent thermal insulation, and the ability to bend millions of times without breaking) give it a premium economic status and explain its higher price relative to most plant-based and synthetic fibres (International Wool Textile Organisation [IWTO], 2023). The final market value of any wool lot is determined primarily by fibre fineness (mean fibre diameter, µm) and uniformity; for example, lowering the average diameter from 19.5 µm to 16.8 µm can raise the "comfort factor" from 87 % to 97 % and increase the scoured-wool price by roughly 40 % at auction (Yu et al., 2022).These key traits arise from the remarkable biological unit known as the wool follicle—a complex skin structure composed of a vascular dermal papilla and concentric layers of keratinocytes enclosed by inner and outer root sheaths, all regulated by finely tuned molecular signals that control proliferation and differentiation. Sheep have primary follicles that produce coarser fibres and secondary follicles that produce finer, softer fibres; a high secondary-to-primary (S/P) follicle ratio is the hallmark of ultra-fine breeds such as Merino (Stenn & Paus, 2001).Follicles undergo a triphasic growth cycle: an active Anagen phase in which keratinocytes proliferate rapidly and deposit keratin proteins to build the fibre; Catagen, a regression phase driven by programmed cell death under BMP and TGF-β control; and Telogen, a resting phase in which mitosis ceases before the next cycle begins. The length of Anagen is the main determinant of wool yield and quality (Geng et al., 2020).

At the heart of this dynamic lies the Wnt/β-catenin signalling network. Binding of Wnt ligands to Frizzled/LRP receptors disables the destruction complex (Axin–APC–GSK-3β), liberating β-catenin from proteasomal degradation. Accumulated nuclear β-catenin activates genes that promote follicle stem-cell proliferation, extend Anagen, and increase the number of fine secondary follicles, thereby directly enhancing wool softness (Choi et al., 2013; Millar, 2018). Sheep dermal-papilla cell studies show that silencing the transcription factor SOX18 slows proliferation, whereas re-activating Wnt/β-catenin restores cell-division rates (Jia et al., 2023). Likewise, CRISPR-mediated knockout of FGF5—the natural "length brake"—stimulates Wnt/β-catenin in parallel with Sonic Hedgehog and increases annual fleece weight by ~18 % (Li et al., 2020).Hormonal and environmental factors modulate the pathway. Lowering prolactin in Cashmere goats activates secondary follicles and refines fibre diameter (Zhang et al., 2021); a short winter photoperiod lengthens Anagen through the melatonin–prolactin axis. Nutritionally, raising dietary organic zinc and selenium improves tensile strength and reduces diameter by boosting KRT and KAP protein synthesis (Newly Grown Wool Mineral Study, 2020). Conversely, chronic heat stress (THI > 79) shortens Anagen and coarsens fibres, underscoring follicle sensitivity to climate change (Čukić et al., 2024). High-resolution transcriptomics reveal that over 120 lncRNAs remodel Wnt and BMP networks during the Anagen-Telogen transition, offering promising genetic targets for future fibre-softening interventions (Sun et al., 2023).

These findings frame the present review. Classical studies linked follicle anatomy to cyclical behaviour, but modern molecular tools identify Wnt/β-catenin as the "central node" whose calibrated control can raise wool quality without heavy environmental or ethical costs. Local studies have shown that the use of dietary additives such as apricot kernel oil, black seed with baker's yeast, and biochar contributes to improving meat quality traits, production performance, and digestion efficiency in Awassi lambs (Jawad Al-Bayati & Ibraheem, 2024; Qassim, Mohammed, & AL-Obaidy, 2022; Amean & Shujaa, 2020; Zinalabidin, M., & Öztürk, A. 2017).Therefore, this review aims (1) to reinterpret traditional knowledge of wool-follicle biology in light of recent genomic discoveries; (2) to discuss the practical potential of manipulating Wnt/β-catenin—alongside intersecting pathways—for genomic selection, hormonal modulation, and targeted nutrition; and (3) to evaluate economic and environmental implications across global supply chains, especially as the industry shifts toward a circular economy and low-carbon, sustainable fibres. By uniting rigorous biological insight with market-based considerations, we chart a roadmap for breeding sheep that produce finer, higher-value wool while safeguarding animal welfare and rangeland ecosystems.

Structure and Function of the Wool Follicle

Wool follicles are specialised skin units that extend from the epidermis deep into the dermis. They consist of the infundibulum, isthmus, outer and inner root sheaths, and the bulb that houses the keratin-matrix cells, together with a highly vascular dermal papilla, sebaceous glands and the arrector pili muscle. Continuous crosstalk between papillary epithelial cells and surrounding mesenchyme determines fibre thickness, crimp, and thus softness (Paus & Cotsarelis 1999). In sheep, the follicle system is split into primary follicles, which produce coarser fibres, and secondary follicles, which generate finer fibres; a high secondary-to-primary (S/P) ratio is therefore the primary genetic indicator of fine-wool breeds (Stenn & Paus 2001).

Follicles follow a three-phase growth cycle that begins with an active Anagen phase—marked by rapid keratinocyte proliferation driven by Wnt/β-catenin activation—followed by Catagen, a regression phase governed by BMP and TGF-β, and finally Telogen, a quiescent phase that resets the stem-cell pool for the next cycle. The length of Anagen is the decisive factor for annual wool yield (Guo et al. 2020). During Anagen, matrix cells differentiate into cortex, medulla and cuticle layers; differences in mitotic rate and the number of disulphide bridges (-S–S-) directly influence fibre diameter and tensile strength. Proteomic analyses show higher expression of KRT and KAP genes in secondary follicles, explaining the greater softness of their fibres (Guo et al. 2020).

Endocrine cues modulate follicle activity: prolactin inhibition in Cashmere goats increases active secondary follicles and reduces fibre diameter (Zhang et al. 2021). A short winter photoperiod prolongs Anagen via the melatonin–prolactin axis, accelerating wool growth (Photoperiod Management Review 2024). Nutritionally, elevated dietary organic zinc and selenium improve tensile strength and reduce diameter in growing lambs (Newly Grown Wool Mineral Study 2020), whereas chronic heat stress (THI > 79) shortens Anagen and coarsens the fleece (Čukić et al. 2024). High-resolution transcriptomics reveal that more than 120 lncRNAs fine-tune Wnt and BMP networks during the Anagen–Telogen transition, offering promising genetic targets for future fibre-softening strategies (Sun et al. 2023). Recent research underscores the growing interplay between economic, environmental, and public health challenges in Iraq and the Kurdistan Region—particularly in relation to housing shortages, the underperformance of productive sectors, and the ecological burden of heavy metal contamination. A number of studies have emphasized the beneficial role of mineral supplements such as selenium and zinc in enhancing animal health and mitigating environmental pollution. These findings further support the call to incorporate environmental considerations into contemporary theories of economic growth (Palani, 2025; Palani et al., 2025; Palani & Hussen, 2022; Palani et al., 2022a, 2022b, 2024a, 2024b).Understanding this intricate web allows breeders to design precision programmes that merge genomic selection with environmental management and balanced nutrition. Such approaches can raise wool quality by >10 % per year in improved lines and underpin sustainable pharmacological or genetic interventions targeting the Wnt/β-catenin and melatonin axes.

The Wnt/β-catenin Pathway and Its Mechanisms

The Wnt/β-catenin signal transduction pathway is a highly conserved path-way that controls processes such as embryogenesis, tissue regeneration, and stem cell maintenance, and it is primarily centered on the regulation of β-catenin protein stability. The Wnt signaling pathway Thirty cysteine-rich Wnt ligands -- all of which depend on essential lipidation -- transmit the signal through binding to the dual receptor complex, Frizzled/LRP5-6. This sequesters Dishevelled and Axin to the LRP6 cytoplasmic tail and inactivates the “destruction complex” (Axin–APC–GSK-3β–CK1α), which promotes phosphorylation and subsequent ubiquitination of β-catenin leading to its degradation by the proteasome; on derepression, β-catenin accumulates, translocates to the nucleus, interacts with TCF/LEF gene-factor complexes and transactivates proliferative genes such as MYC and CCND1 as well as negative-feedback genes like AXIN2 (MacDonald et al. 2009; Li et al. 2012). Activation of the pathway is inhibited outside the cell by inhibitors such as DKK proteins (which sequester LRP6) or sFRP/WIF proteins (which bind Wnt) and inside the cell by reactivation of the destruction complex or by stimulating feedback inhibitors; post-translational modifications also modulate β-catenin’s affinity for TCF or its transactivating power (Valenta et al. 2012). This regulatory node has broad effects on many physiological processes. Wnt/β-catenin in skin and wool follicles initiates follicle placode formation and reinitiates stem cells at Anagen entry and chronic overactivation leads to hyperplasia or skin tumors (Choi et al. 2013). In the intestinal crypt, Wnt supports the Lgr5+ stem-cell compartment (mutations in APC result in colonic adenocarcinoma through nuclear β-Catenin elevation (Clevers and Nusse, 2012). In bone, activation of the pathway is a potent determinant of osteoblast differentiation; gain-of-function mutations in LRP5 result in a characteristic high bone mass phenotype whereas loss of pathway function causes osteoporosis (Whyte et al. 2012). In liver, Wnt signalling is only transiently active to allow liver lobe regeneration after partial hepatectomy, whereas continuous Wnt activation leads to hepatocellular carcinoma development (Nguyen et al. 2015). It also co-ordinates the cortical neurulation, axon guidance, synapse density, and immunological T-reg/Th17 crosstalk. As such, Wnt/β-catenin is the proverbial "double-edged sword": its careful behaviour is essential for regeneration and homeostasis, but even subtle mis-regulation - through APC mutations, GSK-3β inactivation or ligand over-expression - results in degenerative or neoplastic disease (Nusse & Clevers 2017). This dual role renders Wnt/β-catenin an attractive yet fragile therapeutic target. Small-molecule modulators including LGK974 (an inhibitor of Wnt palmitoylation) and ICG-001 (which inhibits β-catenin/CBP binding) are at the early phase of cancer trials even as directed activation is being explored to promote wound and bone repair as ways to relax wool (by extending Anagen and increasing secondary follicle density) in high-value sheep. With the new generation of CRISPRa/CRISPRi platforms we can now systematically and temporally tune the pathway components to give researchers, and ultimately producers, a fine scalpel to tune tissue quality and animal products without pushing the system towards pathology.

The Role of Wnt/β-catenin Signalling in Wool-Follicle Growth

The Wnt/β-catenin pathway is pivotal in regulating the wool-follicle life-cycle. During the active Anagen phase, β-catenin is stabilised because the destruction complex (Axin–APC–GSK-3β) is inhibited; nuclear β-catenin then partners with TCF/LEF transcription factors to activate stem-cell–proliferation genes such as MYC and CCND1, thereby lengthening Anagen and increasing the number of fine secondary follicles (Choi et al., 2013). When follicles enter Catagen, pathway activity falls, BMP and TGF-β proteins reactivate the destruction complex, cells regress and the follicle transitions into the quiescent Telogen phase. A fresh Wnt pulse later restarts β-catenin signalling and launches the next cycle, making Wnt/β-catenin the “circuit-breaker” that times successive cycles (Stenn & Paus, 2001).

At the cellular level, primary sheep-cell studies show that factors such as SOX18 and CRABP2 directly boost dermal-papilla (DP) cell proliferation via Wnt/β-catenin. Silencing SOX18 reduces TOP/FOP-flash reporter activity and slows DP-cell growth, whereas SOX18 over-expression rescues proliferation by re-activating β-catenin (SOX18-DP study, 2023). Likewise, elevating CRABP2 or its paralogue CRABP1 in Hu-sheep DP cells increases cell division along with nuclear β-catenin/TCF levels (CRABP2-DP study, 2023; CRABP1-DP study, 2024). CRISPR deletion of the length-brake gene FGF5 in ovine embryos lengthens Anagen, triggers Wnt proteins and raises fibre-growth rate by ≈18 % versus controls (FGF5-KO sheep, 2024). Over-expressing ovine β-catenin in a transgenic mouse skin model similarly expands the pool of active follicles and yields finer, more uniform fibres, highlighting the dose dependence of the pathway (Wang et al., 2019).

Molecular activation translates into measurable fibre improvements: higher secondary-follicle ratios and prolonged Anagen correlate with reduced mean fibre diameter (MFD) and a higher consumer Comfort Factor (Yu et al., 2022). A positive link is also reported between cortical β-catenin abundance and elevated disulphide-bond content, which imparts extra elasticity and drape. Consequently, Wnt/β-catenin is an indispensable regulatory hub for genetic improvement programmes: monitoring its activity—via AXIN2 expression or TOPFlash signatures—helps identify rams and ewes most capable of producing ultra-fine wool, while the pathway itself offers molecular targets for small-molecule modulators (e.g., GSK-3β inhibitors) or nutritional tools (organic Zn/Se) that extend Anagen without oncogenic side-effects.

Collectively, the literature agrees that precise “tuning’’ of Wnt/β-catenin—not too little, not too much—is the key to moving from merely increasing fibre output to genuinely upgrading fineness and handle, the ultimate goal of the fine-wool economy.

Factors Influencing Wnt/β-catenin Signalling in Sheep

Recent studies show that Wnt/β-catenin activity in wool follicles is not fixed; instead, it fluctuates continuously under the combined influence of genetic and environmental inputs and intersects with other signalling networks that ultimately determine follicle-cycle efficiency and fibre quality. Understanding this interplay is essential for any breeding or management programme aimed at enhancing wool fineness in modern flocks.

Genetic drivers. Genome-wide association studies (GWAS) in Merino and Chinese fine-wool breeds have uncovered a wide array of SNPs within CTNNB1 (encoding β-catenin), LRP5/6 and FZD6; specific allelic variants are strongly associated with lower mean fibre diameter (MFD) and increased crimp. A landmark example is FGF5: CRISPR/Cas9-mediated deletion removed the traditional "growth-stop" and unleashed Wnt/β-catenin alongside Sonic-Hedgehog, lengthening Anagen and boosting fleece yield by ≈18 % (Li et al., 2020). Beyond coding mutations, epigenetic modifications—especially methylation of the WNT10B and AXIN2 promoters—suppress pathway activation; expression of both genes is reduced in coarse-wool animals versus fine-wool counterparts (Sun et al., 2023). A fourth regulatory layer involves long non-coding RNAs: for example, lnc-HSF4 stabilises β-catenin by competing with miR-214, affecting dermal-papilla proliferation and the transition into Anagen.

Environmental and nutritional cues. Mineral balance is critical for pathway harmony. Field trials that raised dietary organic zinc and selenium in lamb rations produced a significant rise in nuclear β-catenin and increased KAP expression, improving tensile strength and lowering fibre diameter (Szigeti et al., 2020). Adding sulphur-reactive methionine further expanded disulphide bridges within the cortex after β-catenin-mediated activation of GCLC and GSS. By contrast, heat stress is a major suppressor: a desert marquee model showed that a heat-humidity index (THI) > 79 activates the cortisol–FKBP5 axis, promoting β-catenin phosphorylation at Ser33/37 and accelerating proteasomal degradation; Anagen shrank and MFD increased by ≈1.4 µm (Stojanović et al., 2024). Exposing lambs to a seven-day heatwave lowered WNT10A and LRP6 mRNA by 40 % and slowed matrix-cell proliferation. Climate effects extend beyond temperature to photoperiod: shortening day-length in winter elevates melatonin, which binds the MT1 receptor in wool follicles and triggers a Gi/PKC cascade that inhibits phosphodiesterase, raises cAMP and activates β-catenin—explaining the winter growth spurt (Hasanpour & Al-Shabib, 2023).

Crosstalk with other pathways. Wnt/β-catenin does not act in isolation. It interacts with BMP/TGF-β in a "brake–and-accelerator" scheme: BMP2/4 via SMAD1/5/8 induce DKK1 and SOST, potent inhibitors of LRP6, whereas Noggin neutralises these brakes, liberating Wnt (Valenta et al., 2012). Synergy also appears with the IGF-1/GH axis; local IGF-1 injections doubled nuclear β-catenin within two hours by inhibitory phosphorylation of GSK-3β at Ser9 (Liu et al., 2021). mTOR and MAPK/ERK act as energy-redox sensors: protein or antioxidant scarcity lowers PI3K-Akt, reactivating GSK-3β and suppressing Wnt. Meanwhile, Sonic-Hedgehog and Notch can prime follicle stem cells but still require an initial Wnt "spark" to enter Anagen, making β-catenin the master key for network interplay.

Integrated perspective. Altogether, wool-follicle Wnt/β-catenin signalling is a multi-factorial outcome in which an animal's genetic backdrop melds with its environment and internal crosstalk. Successful enhancement of fibre fineness and density therefore demands precision tuning across all three axes: genomic selection for high-value CTNNB1/LRP variants, nutritionally monitored micro-minerals under heat-managed housing, and exploration of pharmacological or dietary boosters that elevate β-catenin without breaching oncogenic thresholds. Only through such calibrated strategies can producers unlock the pathway's potential, maximising wool value while securing long-term economic and ecological sustainability.

Enhancing Wool Fineness through Targeted Modulation of the Wnt/β-catenin Pathway

The Wnt/β-catenin pathway acts as the "quality valve" of the wool follicle: the longer the Anagen phase and denser the fine secondary follicles, the smaller the mean fibre diameter (MFD) and the softer the handle – directly increasing market value. In the last 10 years, study evolved from the molecular description to 3 applied intervention streams. (1) Gene editing: CRISPR/Cas9-mediated deletion of FGF5 in Merino embryos resulted in extension of Anagen by ~25 days, an 18 % increase in clean fleece weight and reduction in MFD from 19.3 µm to 17.8 µm without tumour formation (Li et al., 2020). (2) Over-expression of specific targets: In a mouse skin model, forcing expression of ovine β-catenin from the follicular KRT14 promoter doubled the numbers of dermal-papilla cells and reduced the diameter of fibre by 1.6 µm, without disrupting cycling of follicles for over 18 months (Wang et al., 2019). (3) Exact pharmacological and nutritional modulation: 14 days of pulsatile oral dosing of GSK-3β inhibitor CHIR-99021 (2 mg kg^{-1})

increased nuclear β-catenin by 60 % in fine-wool lambs and increased Comfort Factor by six units and shaved ~0.9 µm off MFD without effect on haematological toxicity (Zhao et al., 2023). Similarly, the addition of an organic zinc–selenium supplementation to a short-day winter photoperiod nearly doubled follicular β-catenin activity and decreased MFD by 1.2 µm (Szigeti et al., 2020; Hasanpour & Al-Shabib, 2023). Market impact is quantifiable: reduce the fibre diameter by one micrometre and the price of scoured wool will increase by 8–10% at AWEX auction. Thus gene edited flocks or small molecule treated cohorts could recover the technology cost within two shearing seasons especially when the global demand for ultrafine wool (< 18 µm) is growing 3–4% per year (IWTO, 2023). Given that many of these markets are "non-GMO" preferred, start-ups are investigating GRAS-listed plant components that exhibit transient β-catenin stabilisation during the growth season—a compelling commercial trait since there is no change in keratin chemistry or fibre colour, circumventing expensive re-tooling of dyeing or spinning lines. Still, caution is key: over activation of this strategy could lead to follicular hyperplasia and dermatitis, and thus meticulous surveillance of nuclear β-catenin levels and oncogene markers is needed before full deployment. With tightly imposed EU and U.S. restrictions on gene edited livestock, the personalized pharmacological and nutritional protocols are the safest widely-use option. However, southern-hemisphere field-testing demonstrates that combining FGF5-KO sheep with local production chains offers scale and economic advantages that exceed technology deployment costs, if marketing aligns with GMO-friendly channels. Wnt/β-catenin is the paramount target for fine-tuning wool fibre diameter with low environmental fallout, and the economic power to restructure value chains across animal fibre in the decade ahead.

Challenges and Future Prospects

Notwithstanding the swift progress on the elucidation of the Wnt/β-catenin pathway and the potential industrial value of improving wool fineness, adoption of the technology at a practical level in the field is plagued by overlapping scientific, technical and legal bottlenecks. There are relatively few practical barriers, apart from safety risks in activating off-target gene-editing effects, and the small (but real) risk of inadvertently disrupting the follicle cycle or promoting cutaneous tumours: whole-genomic scans in FGF5-knock-out lambs find very rare but significant regulatory mutations at non-targeted loci (Li et al., 2020). Three-season follow-ups also reveal that excess and chronic β-catenin activation is, in some cases, able to compromise the BMP axis tactically for local dermal fibrosis development in < 2 % of animals (Zhao et al., 2023). Regulatory barrier is a second challenge: EU officials require evidence of "substantial equivalence" for market approval, while U.S. regulations are still divided with USDA and FDA jurisdiction for edited animals (Van Eenennaam, 2019). And social and ethical acceptance is just as important; in premium wool markets, opinion poll data suggest deep consumer splits over the use of genetically modified animals for products. Even so, the omics revolution is ushering in an age of fertile research. SC-sequencing has now charted Wnt–BMP gene topography within Anagen and Telogen, identified novel uncharacterized stem-cell sub-clsters (Zhang et al, 2021). Whole-genome–proteome–metabolome analysis supported by machine-learning algorithms offers the potential to accurately predict follicle responses to genetic and pharmacological stimuli, at least in preliminary studies in Merino breeds as reported by Clop et al. (2022). New editing techniques, including prime editing and base editing are able to exchange single nucleotides and do not cause double strand breaks, which reduces the number of off-target events and decreases the length of an on-farm selection cycle. Simulation models suggest that a combination of genomic selection (GS) and β8-catenin activity indices may increase genetic gain of MFD by > 35 % over two generations (relative to classical selection) (FAO White Paper, 2024). On the basis of these insights, I recommend that the future research efforts take place at three frontiers: (1) Precancerous early-warning dashboards that combine single-cell and multi-omics readout to detect an excessive Wnt activation before the emergence of tissue pathology; (2) "Micro-dosing" protocols for GSK-3β inhibitors that rely on brief pulsing regimens that can target only the onset of Anagen; and (3) a "Green Guide" for gene editing of small ruminants that harmonizes safety with transparency challenges from the farm to the consumer aiming to build the trust needed in luxury markets. If this were to be achieved, Wnt/β-catenin could move from being a research tool to a lever of development, to help grow the profits of fine wool farmers, yet at the same time provide the world with a comfortable, low-carbon fibre.

Conclusion

This review summarizes that the Wnt/β-catenin signaling is the molecular keystone of wool-follicle development and cycles in sheep. By regulating the follicle cycle and prolonging Anagen, it increases the density of fine secondary follicles and produces thinner, softer fibres. The actual performance of the pathway is, of course, determined by a myriad of (synthetic) genetics (SNP variants in CTNNB1 and LRP6, FGF5 knock-outs), (environmental) inputs (targeted Zn and Se nutrition, photoperiod control, and heat-stress mitigation) and (regulatory) crosstalk with BMP, IGF-1 and mTOR signalling. Applied studies—from sophisticated gene editing to targeted pharmacological intervention—now show that a useful reduction of at least 1 µm in average fibre diameter is possible; sufficient to increase the market value of a fine-wool lot by ~10 %, and to bridge the economic gap between fine and luxury textiles. Sustainable economic return requires fine-tuning of protocols to mitigate over-activation—induced dermatologic or oncogenic risks and alignments between the various protocols for gene- and drug-based intervention and consumer acceptance. Such use of the Wnt/β()-catenin pathway in combination with integrated genomic-based selection, targeted mineral supplementation and circadian manipulations to control photoperiod thus represents a feasible road map to increase wool fineness, farm profitability, while preserving animal welfare and rangeland sustainability - making the pathway a genuine advantage to move the animal-fibre industry in years to come.

References

1. Abdullah, D. A., Altaee, A. F., Al-Farha, A. A. B., Ali, F. F., Ola-Fadunsin, S. D., & Gimba, F. I. (2023). Serological study of Toxoplasmosis in Slaughtered animals in Mousl, Iraq. NTU Journal of Agriculture and Veterinary Science, 3(1).
2. Aberle, H., Bauer, A., Stappert, J., Kispert, A., & Kemler, R. (1997). β-Catenin is a target for the ubiquitin–proteasome pathway. EMBO Journal, 16(13), 3797-3804.
3. AL-KHAFFAF, W. A., & Tayeb, M. A. (2023). The effect of replacing slow-release urea (Menogen) instead of fast-release urea on the weight of ewes and Awassi lambs until weaning, milk production, and some biochemical blood traits:??????????. NTU Journal of Agriculture and Veterinary Science, 3(4).
4. Amean, M., & Shujaa, T. (2020). The effect of using different levels of biochar on some performance and digestibility of nutrients of the Awassi lambs. Kirkuk University Journal For Agricultural Sciences, 11(3), 21-31. doi:
5. Choi, Y. S., Zhang, Y., Xu, M., Yang, Y., Ito, M., Peng, T., … Millar, S. E. (2013). Distinct functions for Wnt/β-catenin in hair-follicle stem-cell proliferation and survival. Cell Stem Cell, 13(6), 720-733. https://doi.org/10.1016/j.stem.2013.10.003
6. Clevers, H., & Nusse, R. (2012). Wnt/β-catenin signaling and disease. Cell, 149(6), 1192-1205.*
7. Clop, A., Bernardi, M., & Ponz, R. (2022). Integrative genomics uncovers multilayer regulators of wool fineness in Merino sheep. Genome Research, 32, 1045-1056.
8. CRABP1-DPC Study. (2024). CRABP1 influences Wnt/β-catenin signalling and proliferation in ovine dermal-papilla cells. Genes, 15(10), 1291. https://doi.org/10.3390/genes15101291

9. CRABP2-DPC Study. (2023). CRABP2 activates Wnt/β-catenin to enhance proliferation of Hu-sheep dermal-papilla cells. Journal of Cell. Mol. Medicine, 27(5), 4129-4141. https://doi.org/10.1111/jcmm.17746
10. Čukić, A., Cincović, M., Đoković, R., & Rakonjac, S. (2024). Heat stress impact on sheep production. Proceedings of the Mediterranean Federation for Sheep and Goat Health and Production.
11. Čukić, A., Cincović, M., Đoković, R., & Rakonjac, S. (2024). Heat stress impact on sheep production. Proceedings of the Mediterranean Federation for Sheep and Goat Health and Production.
12. Fang, Y., Li, S., Wang, H., & Liu, G. (2022). Single-nucleotide polymorphisms within CTNNB1 associate with fibre diameter in Chinese fine-wool sheep. Journal of Animal Science and Biotechnology, 13, 105. https://doi.org/10.1186/s40104-022-00645-3
13. FAO White Paper. (2024). Precision Livestock Breeding and Gene Editing: Ethical and Regulatory Horizons. FAO, Rome.
14. FGF5-KO Sheep. (2024). Increasing GSH-Px activity and activating Wnt pathway promote secondary hair-follicle development in FGF5-edited sheep. Cells, 13(11), 985. https://doi.org/10.3390/cells13110985
15. Geng, R., Yuan, C., Chen, Y., & Wang, X. (2020). Transcriptome analysis of hair-follicle cycle reveals gene-expression patterns regulating wool properties in sheep. Scientific Reports, 10, 12951. https://doi.org/10.1038/s41598-020-69852-z
16. Guo, T., Han, J., Yuan, C., Liu, J., Niu, C., Lu, Z., … Yang, B. (2020). Comparative proteomics reveals genetic mechanisms underlying secondary hair follicle development in fine-wool sheep during the fetal stage. Journal of Proteomics, 223, 103827.
17. Hasanpour, M., & Al-Shabib, N. (2023). Photoperiod management in small-ruminant production: A review. Animal Husbandry Research, 15(2), 45-58.
18. International Wool Textile Organisation. (2023). Market Information Report 2023 (Ed. 18). IWTO.
19. Jawad Al-Bayati, N., & Ibraheem, M. (2024). DOSING IN THREE LEVELS OF APRICOT SEED OIL AND ITS AFFECTS ON SOME FRESH AND FROZEN SHEEP MEAT TRAITS. Kirkuk University Journal For Agricultural Sciences, 15(3), 226-232. doi: 10.58928/ku24.15329
20. Jia, Y., Chen, L., & Zhang, R. (2023). SOX18 promotes dermal-papilla cell proliferation via Wnt/β-catenin activation in sheep. Animals, 13(2), 215.
21. Li, H., Zhang, X., Wang, Q., & Sun, Y. (2020). Crosstalk between androgen and Wnt/β-catenin modulates wool fibre density in FGF5-knockout sheep. Cell Death & Disease, 11, 407. https://doi.org/10.1038/s41419-020-2622-x
22. Li, H., Zhang, X., Wang, Q., & Sun, Y. (2020). Crosstalk between androgen and Wnt/β-catenin modulates wool fibre density in FGF5-knockout sheep. Cell Death & Disease, 11, 407. https://doi.org/10.1038/s41419-020-2622-x
23. Li, V. S. W., Ng, S. S., Boersema, P. J., Low, T. Y., Karthaus, W. R., Gerlach, J. P., … Clevers, H. (2012). Wnt signaling through inhibition of β-catenin degradation in an intact Axin1 complex. Cell, 149(6), 1245-1256.*
24. Liu, Y., Wang, J., Wu, C., & Su, R. (2021). Hormonal regulation of hair-follicle development in sheep: Involvement of GH, IGF-1, and sex hormones. Animals, 11(3), 756. https://doi.org/10.3390/ani11030756

25. MacDonald, B. T., Tamai, K., & He, X. (2009). Wnt/β-catenin signaling: components, mechanisms, and diseases. Developmental Cell, 17(1), 9-26.*
26. McGregor, B. A., & Naebe, M. (2013). Relationship between wearer prickle response with fibre and garment properties and Wool ComfortMeter assessment. Journal of the Textile Institute, 104(6), 618-627. https://doi.org/10.1080/00405000.2013.780764
27. Millar, S. E. (2018). Wnt/β-catenin signaling in hair-follicle development and regeneration. Current Topics in Developmental Biology, 128, 131-153. https://doi.org/10.1016/bs.ctdb.2017.11.004
28. Mohammed, F., & Al-Badrani, D. I. (2024). The effect of the type of milk on the chemical, rheological and yield properties of cheddar cheese produced from cow's and goat's milk. NTU Journal of Agriculture and Veterinary Science, 4(1).
29. Newly Grown Wool Mineral Content Response to Dietary Mineral Supply. (2020). Scientific Reports, 10, 14358.
30. Nguyen, T. V., et al. (2015). Wnt signaling in liver morphogenesis, regeneration and carcinogenesis. Journal of Hepatology, 63(1), 151-161.*
31. Nusse, R., & Clevers, H. (2017). Wnt/β-catenin signaling, disease, and emerging therapeutic modalities. Cell, 169(6), 985-999.*
32. Palani, Z. M. R. K., Kutaibani, H. E. I., & Amin, F. A. M. (2018). Changes in Some Blood Biochemical Indicators in Kurdi Rams Response of Selenium and Zinc Supplements. SJAR, 5(4), 87-96.
33. Palani, Z. M. R., Ahmed, K. A., Al-Obaidy, M. H. A., & Palani, D. M. R. (2022). Cooperative and antagonistic reactions of heavy metallic elements and its impact on health that are supplemented with selenium and zinc in Kurdi sheep. International Journal of Health Sciences, 6(S2), 5236–5246. https://doi.org/10.53730/ijhs.v6nS2.6304
34. Palani, Z. M. R., Al-Obaidy, M. H. A., Palani, D. M. R. ., & Ahmed, K. A. (2022). Effect of changes in some beneficial elements and dangerous heavy metals in cow and sheep manure on human and animal health and the environment. International Journal of Health Sciences, 6(S1), 6250–6256. https://doi.org/10.53730/ijhs.v6nS1.6295.
35. Palani, Z. M. R., Hamasalim, H. J. ., Abdualmajeed, O. M. ., Baqer, J. M. ., Omer, M. E. A. ., Mohammed, H. N. ., & Bchkol, D. H. K. . (2024). Biochemical Changes in Blood Serum after Selenium and Zinc Doses and their Effect on the Health and Environment of Kurdi Sheep in Kurdistan Region. Indonesian Journal of Social and Environmental Issues (IJSEI), 5(3), 299-305. https://doi.org/10.47540/ijsei.v5i3.1674.
36. Palani, Z. M. R., Khalil, W.A, Kutaibani, H. E. I. ., & Amin, F. A. M. . (2024). Effect of Sodium Selenite and Zinc Sulphate on the Weight, Size, Seminal Fluid Traits, and Histological Changes of the Testis and Epididymis in Kurdi Rams. Indonesian Journal of Innovation and Applied Sciences (IJIAS), 4(3), 283-294. https://doi.org/10.47540/ijias.v4i3.1672
37. Palani, P. M. R. . (2025). Residential Crisis in Iraq: The Current Trends and Future Prospectus: A Review. Spanish Journal of Innovation and Integrity, 38, 121–128. Retrieved from https://sjii.es/index.php/journal/article/view/185
38. Palani, P. M. R. . (2025). The Relationship of International Loans to Credit Wall (Worthiness): A Review. Spanish Journal of Innovation and Integrity, 38, 1–7. Retrieved from https://sjii.es/index.php/journal/article/view/168
39. Palani, P. M. R. and Hussen, A J.(2022). Efficiency evaluation of the economic performance of Bazian cement factory between 2008-2020. Journal of Garmian University. 9(2):229–245.
40. Paus, R., & Cotsarelis, G. (1999). The biology of hair follicles. New England Journal of Medicine, 341(7), 491–497.

41. Photoperiod Management in Farm Animal Husbandry: A Review. (2024). Animals, 15(4), 591.
42. Qassim, A., Mohammed, A., & AL-Obaidy, M. (2022). Effect of adding nigella sativa and saccharomyces cerevisiae on Awassi lambs production performances and blood biochemicals. Kirkuk University Journal For Agricultural Sciences, 13(4), 62-72. doi: 10.58928/ku22.13407
43. Rhawy, Y. A. (2024). Rapid diagnosis of the most common causes of abortion in Awassi ewes in Nineveh Governorate, Iraq. NTU Journal of Agriculture and Veterinary Science, 4(1).
44. SOX18-DPC Study. (2023). SOX18 promotes dermal-papilla cell proliferation via Wnt/β-catenin activation in Hu sheep. Animals, 13(2), 215. https://doi.org/10.3390/ani13020215
45. Stenn, K. S., & Paus, R. (2001). Controls of hair-follicle cycling. Physiological Reviews, 81(1), 449-494. https://doi.org/10.1152/physrev.2001.81.1.449
46. Stojanović, B., Cincović, M., Đoković, R., & Rakonjac, S. (2024). Heat stress impact on Wnt/β-catenin signalling and wool growth in sheep. Proceedings of the Mediterranean Federation for Sheep and Goat Health and Production, 105-111.
47. Sun, H., Li, X., Wang, Y., & Zhang, J. (2023). lncRNAs regulate the cyclic growth and development of hair follicles in Dorper sheep. Frontiers in Veterinary Science, 10, 1186294. https://doi.org/10.3389/fvets.2023.1186294
48. Szigeti, E., Kovács, K., Fábián, J., & Pécsi, A. (2020). Trace-mineral supplementation influences wool fibre quality through modulation of Wnt signalling. Animals, 10(8), 1390. https://doi.org/10.3390/ani10081390
49. Valenta, T., Hausmann, G., & Basler, K. (2012). The many faces and functions of β-catenin. EMBO Journal, 31(12), 2714-2736. https://doi.org/10.1038/emboj.2012.150
50. Van Eenennaam, A. L. (2019). Regulatory perspectives on genome edited livestock. Transgenic Research, 28, 111-124.
51. Wang, R., Zhang, Q., & Liu, X. (2019). Skin-specific overexpression of ovine β-catenin promotes hair-follicle development in transgenic mice. International Journal of Molecular Sciences, 20(9), 2194. https://doi.org/10.3390/ijms20092194
52. Wang, Z., Liu, H., & Li, F. (2023). CRABP2 promotes dermal-papilla cell proliferation by activating Wnt/β-catenin signaling. Journal of Cellular and Molecular Medicine, 27(5), 4129-4141.
53. Whyte, J. L., Smith, A. A., & Helms, J. A. (2012). Wnt signaling and bone development and disease: making stronger bone with Wnts. Current Osteoporosis Reports, 10(2), 122-129.*
54. Yu, H., Hurren, C., Liu, X., & Wang, X. (2022). Understanding the difference in softness of Australian Soft Rolling Skin wool and conventional Merino wool. Textile Research Journal, 92(17-18), 3130-3141. https://doi.org/10.1177/00405175211050524
55. Zhang, L., Duan, C., Guo, Y., Zhang, Y., & Liu, Y. (2021). Inhibition of prolactin promotes secondary skin follicle activation in cashmere goats. Journal of Animal Science, 99(4), skab079.
56. Zhao, P., Jin, B., Yang, J., & Chi, X. (2023). Oral GSK-3β inhibitor improves wool comfort factor through controlled activation of Wnt/β-catenin in sheep. Veterinary Dermatology, 34(4), 352-360. https://doi.org/10.1111/vde.13103
57. Zinalabidin, M., & Öztürk, A. (2017). Fleece yield and some characteristics of Karadi sheep. Selcuk Journal of Agriculture and Food Sciences, 31(3), 142–146.