Project Notes:

Project Title: Investigating the Role of Canonical Wnt Signaling in Dental Regeneration (With Some Applications to Cancer Treatment)

Name: Lilian Amer

Note Well: There are NO SHORT-cuts to reading journal articles and taking notes from them. Comprehension is paramount. You will most likely need to read it several times, so set aside enough time in your schedule.

Contents:

Knowledge Gaps: 3

Literature Search Parameters: 6

Article #1 Notes: Title 8

Patent #1 Notes: Dental Implant Assembly, Implant, and Prosthesis to Replace a Nonfunctional Natural Tooth and Related Methods 8

Patent #2 Notes: Medical and Dental Biomaterial and method of use for the same 10

Patent #3 Notes: Methods and compositions for dental tissue repair and/or regeneration 10

Patent #4 Notes: Hydrogel bioscaffold and coating for bone and tooth repair 11

Article #2 Notes: Tooth Repair and Regeneration 11

Article #3 Notes: Mesenchymal stromal cell exosomes enhance dental pulp cell functions and promote pulp-dentin regeneration 13

Article #4 Notes: iPSC-derived cranial neural crest-like cells can replicate dental pulp tissue with the aid of angiogenic hydrogel 15

Article #5 Notes: The potential of exosomes from adipose-derived stromal-vascular fraction in Increasing Migration Activity of Human Dental Pulp Stromal Cells (in vitro study) * 17

Article #6 Notes: Stem Cell ‐ based Dental Pulp Regeneration: Insights From Signaling Pathways 19

Article #7 Notes: Basic Fibroblast Growth Factor Regulates Gene and Protein Expression Related to Proliferation, Differentiation, and Matrix Production of Human Dental Pulp Cells 21

Article #8 Notes: Wnt signaling activation: targets and therapeutic opportunities for stem cell therapy and regenerative medicine 23

Article #9 Notes: Effects of different signaling pathways on odontogenic differentiation of dental pulp stem cells: a review 25

Article #10 Notes: Wnt signaling in dental pulp homeostasis and dentin regeneration 27

Article #11 Notes: Non-canonical Wnt signaling participates in Jagged1-induced osteo/odontogenic differentiation in human dental pulp stem cells 29

Article #12 Notes: An insight into planarian regeneration 31

Article #13 Notes: Wnt signaling in planarians: new answers to old questions 32

Article #14 Notes: Topical Application of Lithium Chloride on the Pulp Induces Dentin Regeneration 34

Article #15 Notes: Modulators of Wnt Signaling Pathway Implied in Dentin Pulp Complex Engineering: A Literature Review 36

Article #16 Notes: GSK3 Inhibitor-Induced Dentinogenesis Using a Hydrogel 38

Article #17 Notes: Formaldehyde-based whole-mount in situ hybridization method for planarians 40

Article #18 Notes: Wnt Signaling Inhibitors and Their Promising Role in Tumor Treatment 42

Article #19 Notes: New insight into dental epithelial stem cells: Identification, regulation, and function in tooth homeostasis and repair 44

Article #20 Notes: Wnt3a promotes odonto/osteogenic differentiation in vitro and tertiary dentin formation in a rat model 46

Article #21 Notes: Effects of miR-335-5p in Modulating Osteogenic Differentiation by Specifically Downregulating Wnt Antagonist DKK1 48

Knowledge Gaps:

This list provides a brief overview of the major knowledge gaps for this project, how they were resolved and where to find the information.

Knowledge Gap	Resolved By	Information is located	Date resolved
Background information on current biotech innovations on tooth regeneration	Reading an article on tooth repair and regeneration technology and methods	Article #2	August 15, 2024
Different ways that tooth regeneration can be triggered	Article on mesenchymal stromal cell exosomes and how they aid in tooth regeneration	Article #3	September 3, 2024
Different ways that tooth regeneration can be triggered	Article on the use of CNCLCs to replicate dental pulp tissue and how the process of CNCLC regeneration can be triggered by angiogenic hydrogel	Article #4	September 14, 2024
Use of exosomes on different activity of hDPSCs	Article on exosomes from adipose-derived stromal-vascular fraction and how they play a role on the migration activity of hDPSCs	Article #5	September 14, 2024
How dental pulp regeneration even begins	Learned more about the different signalling pathways and how they affect dental pulp / oral health overall	Article #6	September 22, 2024
Different materials that could help with stem cell tissue regeneration	Studied the role of basic fibroblast growth factors in dental pulp stem cell tissue regeneration	Article #7	September 22, 2024
Specifics on signalling pathways that could	Read up on the role of Wnt signalling pathway in generating more tissue	Article #8	September 23, 2024

help with regenerative medicine as a whole	(how if it's too active, it leads to cancer, too inactive, leads to too little regeneration)		
More on different signalling pathways	Read an article that reviewed 6 different signalling pathways and how they affect oral health	Article #9	September 29, 2024
Details on the Wnt signalling pathway and its specific applications in dentistry	Read up on how it works to regenerate dentin	Article #10	October 6, 2024
Details on the Wnt signalling pathway and its specific applications in dentistry	Read on how non-Canonical Wnt Jagged1 proteins help with osteo/odontogenic differentiation of hDPSCs	Article #11	October 6, 2024
How are planaria used in regenerative medicine research and why	Read an article that discusses the regenerative abilities of planaria + recent discoveries made using planaria	Article #12	October 27, 2024
The effects of Wnt signalling in Planaria specifically (does it even exist in planaria?)	Read an article on its applications in planaria + how recent research has been conducted and yielded answers to questions that researchers had regarding Wnt	Article #13	October 27, 2024
What different chemicals / proteins / other help with the activation of Wnt signalling?	Read an article on the effects of lithium chloride on activating the Wnt signalling pathway + regeneration	Article #14	November 3, 2024
What different chemicals / proteins / other help with the	Read a review article on different modulators of the Wnt signalling	Article #15	November 3, 2024

activation of Wnt signalling?	pathway that aid in dental regeneration		
How can NP928 help with dental regeneration?	Read an article that described the benefits of NP928 as a GSK3-inhibitor on inducing dentinogenesis	Article #16	November 10, 2024
How to measure the blastema growth of the planaria	Read an article on Fiji/ImageJ technology and how to quantify blastema growth using the software	Article #17	November 10, 2024
What different Wnt inhibitors exist? What would they be used for?	Read an article on the inhibitors of Wnt and how they help with tumor treatment	Article #18	November 17, 2024
How does enamel regeneration work?	Read an article on DESCs and how they function to help with the regeneration of enamel	Article #19	November 17, 2024
How does Wnt3A help with dental regeneration?	Read an article on Wnt3A proteins and how they have been shown to aid in dental regeneration by activating the Wnt signalling pathway	Article #20	November 17, 2024
What are some other ways of regenerating the dental pulp?	Read an article on how miR-335-5p helps in modulating osteogenic differentiation	Article #21	November 20, 2024

Literature Search Parameters:

These searches were performed between 15/08/2024 and 06/10/2024.
List of keywords and databases used during this project:

Database/search engine	Keywords	Summary of search
Google Scholar	Tooth Regeneration	Articles give quick reviews of tooth regeneration thus far and talk about why tooth repair / regeneration should be the next focus, as current solutions to tooth decay and tooth loss are not very practical and can cause greater harm in the future.
PUB Med	Dentin regeneration	Articles were about different and current methods of dentin regeneration, most by the usage of stem cells
PUB Med	Dental pulp tissue	Articles found were on different dental pulp tissue regeneration and preservation methods, with the article I read being on how a specific cell can replicate dental pulp tissue
PUB Med	Wnt Signalling dentistry	Most articles were old, but most of them provided information on how research was conducted to see the effectiveness of the Wnt signalling pathway in regenerative dentistry
PUB Med	Planaria	Articles about studies conducted using planaria, mostly focused on regenerative abilities of planaria / how research has advanced since then

Tag Name	
#Intro	#BackgroundInfo
#GeneralInfo	#Exosomes

#DentalPulpRegneration	#SignallingPathways
#WntSignallingPathway	#Pulp-DentinRegeneration
#hDPSCs	#NotchSignalling
#Non-CanonicalWntSignalling	#bFGFs
#Planaria	#WntPlanaria
#DKK1	#Differentiation
#Wnt3A	#Activator
#DentalEpithelialStemCells	#Inhibitor
#CanonicalWntSignalling	#NP928
#Methodology	#DentinRegeneration
#Wedelolactone	#LiCl

Article #1 Notes: Title

Article notes should be on separate sheets

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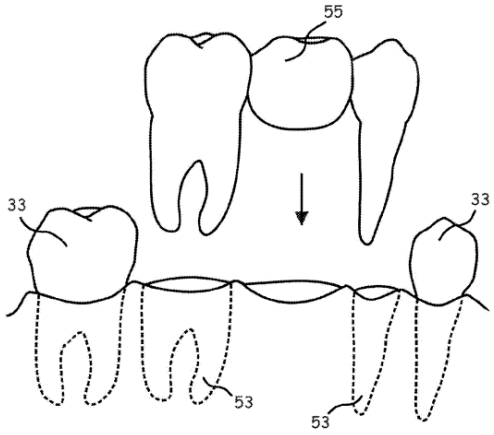
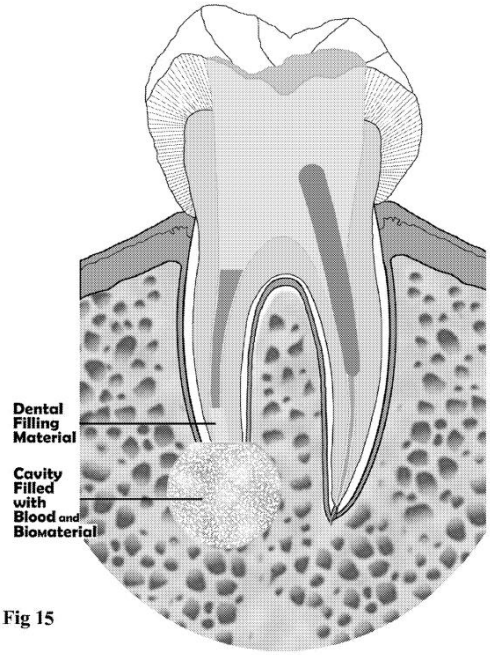
Source Title	
Source citation (APA Format)	
Original URL	
Source type	
Keywords	
#Tags	
Summary of key points + notes (include methodology)	
Research Question/Problem/ Need	
Important Figures	
VOCAB: (w/definition)	
Cited references to follow up on	
Follow up Questions	

Patent #1 Notes: Dental Implant Assembly, Implant, and Prosthesis to Replace a Nonfunctional Natural Tooth and Related Methods

Source Title	Google Scholar
Source citation (APA Format)	Rubbert, R., and Nesbit, L. E. (2013). *Dental Implant Assembly, Implant, and Prosthesis to Replace a Nonfunctional Natural Tooth and Related Methods* (US Patent No. 2013/0209961). U.S. Patent and Trademark Office. https://patentimages.storage.googleapis.com/45/b6/51/f6407089820eab/US2013020996

	1A1.pdf
Original URL	https://patentimages.storage.googleapis.com/45/b6/51/f6407089820eab/US20130209961A1.pdf
Source type	Patent
Summary of key points + notes (include methodology)	The researchers created a dental implant to replace a nonfunctional natural tooth and explored several other methods. They did this by studying a scan they received from a predetermined patient of the tooth cavities and assembled and implanted a dental implant.
Research Question/Problem/ Need	How to create a dental implant that is both effective and comfortable for the patient?
Important Figures	 FIG. 10.

Patent #2 Notes: Medical and Dental Biomaterial and method of use for the same

Source Title	Google Scholar
Source citation (APA Format)	Asgary, S. (2012). *Medical and Dental Biomaterial and method of use for the same (*US Patent 8,105,086). U.S. Patent and Trademark Office. https://patentimages.storage.googleapis.com/28/99/d6/11a9e5c8ca0678/US8105086.pdf
Original URL	https://patentimages.storage.googleapis.com/28/99/d6/11a9e5c8ca0678/US8105086.pdf
Source type	Patent
Summary of key points + notes (include methodology)	The researcher created a biomaterial that can be used in filling or sealing tooth and bone cavities. Several calcium-based compounds were mixed with water while phosphate compounds were prepared, and when mixed, this creates hydroxyapatite. The biomaterial can help stimulate hard / soft tissue healing, generation, or regeneration.
Research Question/Problem / Need	Create a biomaterial that can be used to seal or fill tooth and bone cavities and that can stimulate hard / soft tissue healing, generation, or regeneration.
Important Figures	 Fig 15

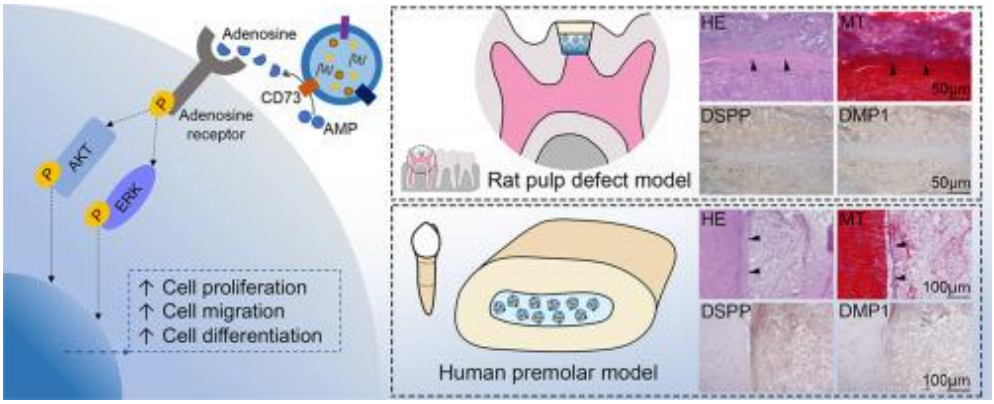
Article #2 Notes: Tooth Repair and Regeneration

Source Title	Springer Link
Source citation (APA Format)	Angelova Volponi, A., Zaugg, L.K., Neves, V., Liu, Y., & Sharpe, P. T. (2018). Tooth Repair and Regeneration. *Current Oral Health Reports*, *5*, 295–303. https://doi.org/10.1007/s40496-018-0196-9
Original URL	https://link.springer.com/article/10.1007/s40496-018-0196-9
Source type	Science Journal
Keywords	Tooth Repair, Tooth Regeneration, Whole-Tooth Bioengineering, Organogenesis
#Tags	#Intro #BackgroundInfo #GeneralInfo
Summary of key points + notes (include methodology)	This review analyzes the different ways in which the field of tooth regeneration has advanced in the past, studying the three approaches of enamel mineralization, whole tooth engineering, and the biological repair of dentin. While osseointegrated dental implants revolutionized dentistry in the past, they lack the periodontal ligament that protects against the mastication force that could cause jawbone resorption, so they aren't sustainable in the long run to a person's oral health. Advances in restorative dentistry focus on repairing or regenerating the tooth enamel and dentine-pulp complexes using biomimetic methods and stem cell therapies, as well as working towards whole tooth bioengineering.
Research Question/Problem/ Need	How has tooth repair and regeneration technology and methods advanced over the past couple of years?
Important Figures	Figure B – shows process of bioengineered tooth implant
VOCAB: (w/definition)	Wnt/β-catenin signaling pathway – biological pathway of cell development and repair. Activating this can stimulate formation of new dentin and support the repair and regeneration of dental tissues, including reactionary and reparative dentine Ameloblasts – cells responsible for forming dental enamel. During tooth development, ameloblasts are active in producing enamel but go through a programmed cell death once the enamel has fully matured, making the enamel incapable of natural repair Odontoblasts – cells in the dental pulp responsible for dentin formation. Can secrete new dentin as part of the tooth's natural repair processes, including reactionary and reparative dentine formation
Cited references to follow up on	Yang L, Angelova Volponi A, Pang Y, Sharpe PT. Mesenchymal cell community effect in whole tooth bioengineering. J Dent Res. 2017;96(2):186–91. https://doi.org/10.1177/0022034516682001. This original research work explores the cell community effect on mesenchymal cells as a tool to "rescue" the odontogenic potential of cultured cells that is lost in vitro.

Follow up Questions	How could the genetic mechanisms in humans be modified to enable the growth of additional permanent teeth beyond the typical one tooth? (more specifically for cells like ameloblasts) How could periodontal ligament be integrated in bioengineered teeth to avoid jawbone resorption? How can bioprinting be used to help with the regeneration or bioengineering of teeth?

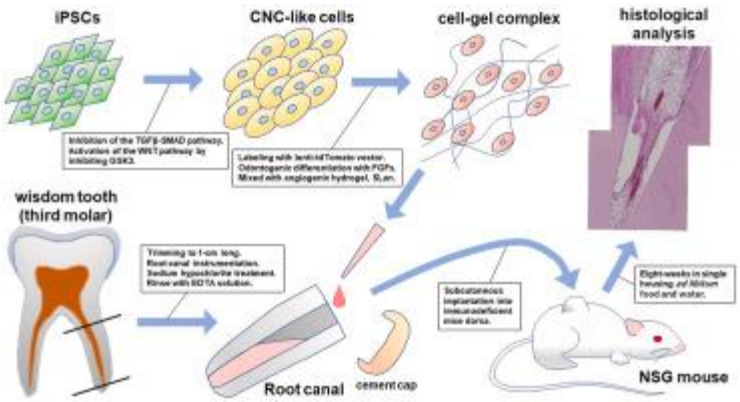
Article #3 Notes: Mesenchymal stromal cell exosomes enhance dental pulp cell functions and promote pulp-dentin regeneration

Source Title	Science Direct
Source citation (APA Format)	Shi, J., Teo, K. Y. W., Zhang, S., Lai, R. C., Rosa, V., Tong, H. J., Duggal, M. S., Lim, S. K., & Toh, W. S. (2023). Mesenchymal stromal cell exosomes enhance dental pulp cell functions and promote pulp-dentin regeneration. *Biomaterials and Biosystems, 11.* https://doi.org/10.1016/j.bbiosy.2023.100078
Original URL	https://www.sciencedirect.com/science/article/pii/S2666534423000077
Source type	Science Journal
Keywords	Pulp-dentin regeneration, mesenchymal stromal cell exosomes, mesenchymal stromal cells, exosomes, stem cells, mesenchymal stem cell therapy, MSCs
#Tags	#Pulp-dentinRegeneration #Exosomes
Summary of key points + notes (include methodology)	The researchers explored how exosomes from mesenchymal stromal cells can help with the reparation of dental pulp by improving the migration, growth, and specialized cell functions of dental pulp cell. These effects are achieved by specific signaling pathways that are activated by exosomes. The study shows that MSC exosomes can promote the formation of dentin-like tissue and repair dental pulp in various models. Methodology: MSC exosomes were prepared from an immortalized E1-MYC 16.3 line derived from human embryonic stem cells (hESCs). Dental pulp cells were isolated from the extracted incisors of 8-week-old female Sprague-Dawley rats. DPCs were treated with different concentrations of exosomes or control solutions. Viability was assessed using MTS and DNA content measurements. Apoptosis in DPCs was evaluated using Annexin V and propidium iodide staining, analyzed by flow cytometry. The migration of DPCs in response to exosome treatment was measured using a transwell system. To study the signaling pathways activated by exosomes, DPCs were pre-treated with various inhibitors before exosome treatment. Effects on the involvement of adenosine receptors and the signaling pathways AKT and ERK were analyzed. In animal models, pulp defects or human premolar roots were treated with exosomes or controls. The data was then analyzed using statistical tests to determine the significance of different experimental conditions
Research Question/Problem/ Need	How can exosomes from MSC therapy enhance dental pulp cell regeneration?

Important Figures	 Graphical abstract
VOCAB: (w/definition)	MSC - Mesenchymal stromal cells (MSCs) are a type of adult stem cell found in various tissues, including bone marrow, fat, and umbilical cord blood. Exosomes - Exosomes are tiny, membrane-bound vesicles released by cells into the extracellular space.
Cited references to follow up on	Preliminary study on dental pulp stem cell-mediated pulp regeneration in canine immature permanent teeth J Endod, 39 (2) (2013), pp. 195-201, 10.1016/j.joen.2012.10.002 Challenges and advances in clinical applications of mesenchymal stromal cells J Hematol Oncol, 14 (1) (2021), p. 24, 10.1186/s13045-021-01037-x
Follow up Questions	What specific molecular mechanisms are involved in the activation of the AKT and ERK signaling pathways by MSC exosomes in dental pulp cells? Are there additional signaling pathways or molecular interactions that could also play a role in the observed effects?

Article #4 Notes: iPSC-derived cranial neural crest-like cells can replicate dental pulp tissue with the aid of angiogenic hydrogel

Source Title	ScienceDirect
Source citation (APA Format)	Kobayashi, Y., Nouet, J., Baljinnyam, E., Siddiqui, Z., Fine, D. H., Fraidenraich, D., Kumar, V. A., & Shimizu, E. (2022). iPSC-derived cranial neural crest-like cells can replicate dental pulp tissue with the aid of angiogenic hydrogel. *Bioactive Materials, 14*, 290–301. https://doi.org/10.1016/j.bioactmat.2021.11.014
Original URL	https://www.sciencedirect.com/science/article/pii/S2452199X21005351
Source type	Scientific Journal
Keywords	Dental pulp tissue, iPSC-derived cranial neural crest-like cells
#Tags	#DentalPulpRegneration
Summary of key points + notes (include methodology)	CNCLCs were used to replicate the characteristics of dental pulp tissue by improving a process that previously existed that used iPSCs. They showed significant odontoblast differentiation ability, particularly when treated with FGFs. A mouse subcutaneous model was used to exhibit the replication of the CNCLCs to the dental pulp tissue characteristics. This was induced by SAPH (angiogenic self-assembling peptide hydrogel) SLan, which is a versatile biocompatible scaffold. SLan was synthesized and prepared using standard solid-phase procedures and purified. Human iPSCs were obtained from human gingival fibroblasts collected from the gingival connective tissue connected to extracted third molars. Root fragments from third molars were prepared and implanted with labeled cells into mice, and after 8 weeks, histological analysis was conducted to assess the pulp regeneration. It was found that the most well-established method for generating neural crest (NC)-like cells from iPSCs involves activating the Wnt signaling pathway. The study shows the success of combining regenerative science with SAPH technology.
Research Question/Problem/ Need	How can the previously existing method for CNCLC replication of dental pulp tissue be improved upon using SLan and SAPH technology?

Important Figures	 Graphical abstract
VOCAB: (w/definition)	Peptides – short chains of amino acids linked by peptide bonds.
Cited references to follow up on	https://www.frontiersin.org/journals/bioengineering-and-biotechnology/articles/10.3389/fbioe.2020.00475/full
Follow up Questions	How do different designs of angiogenic hydrogels affect the replication and functionality of CNCLCs and thus dental pulp tissue?

Article #5 Notes: The potential of exosomes from adipose-derived stromal-vascular fraction in Increasing Migration Activity of Human Dental Pulp Stromal Cells (in vitro study) *

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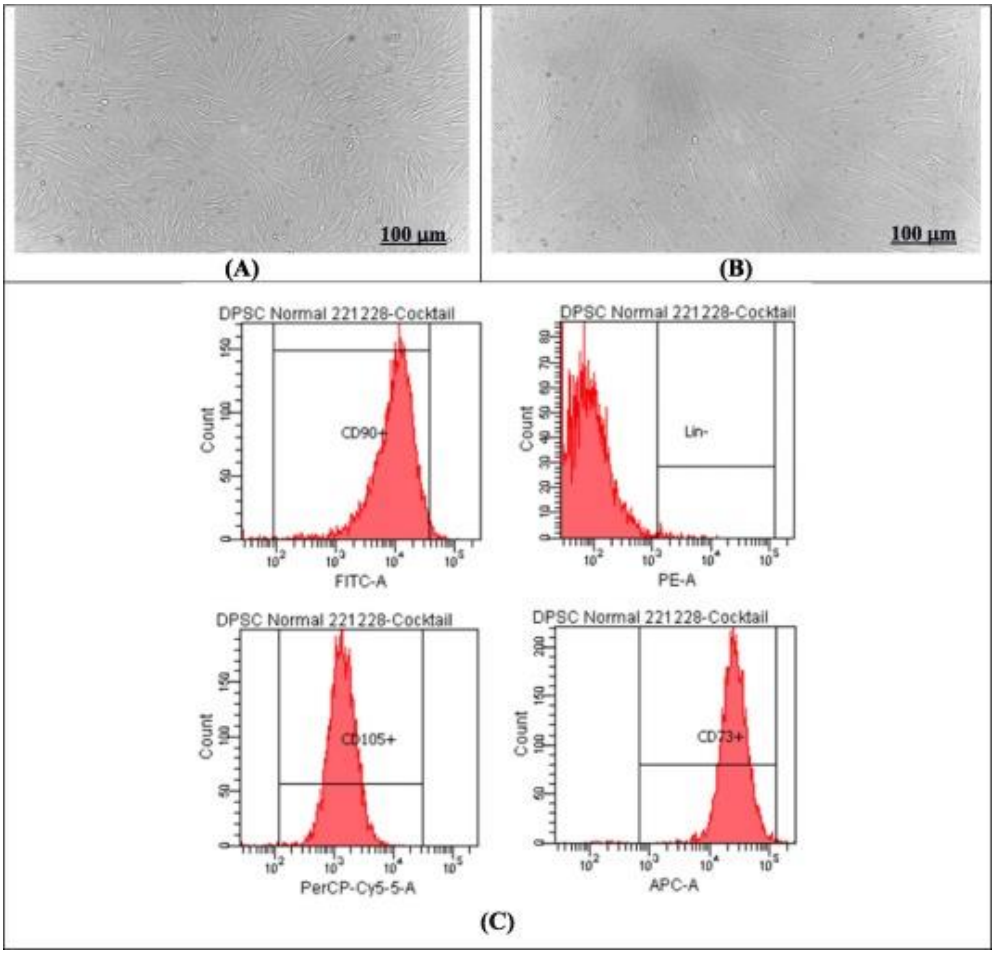
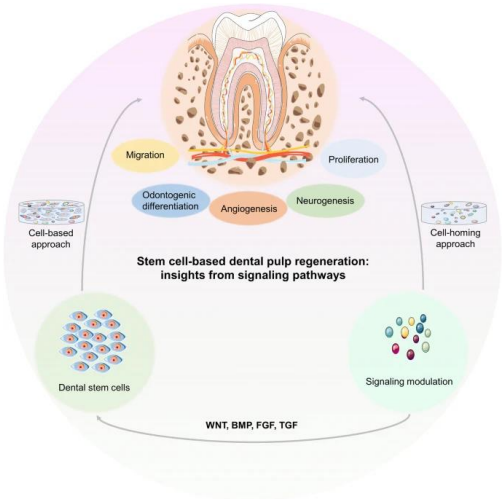
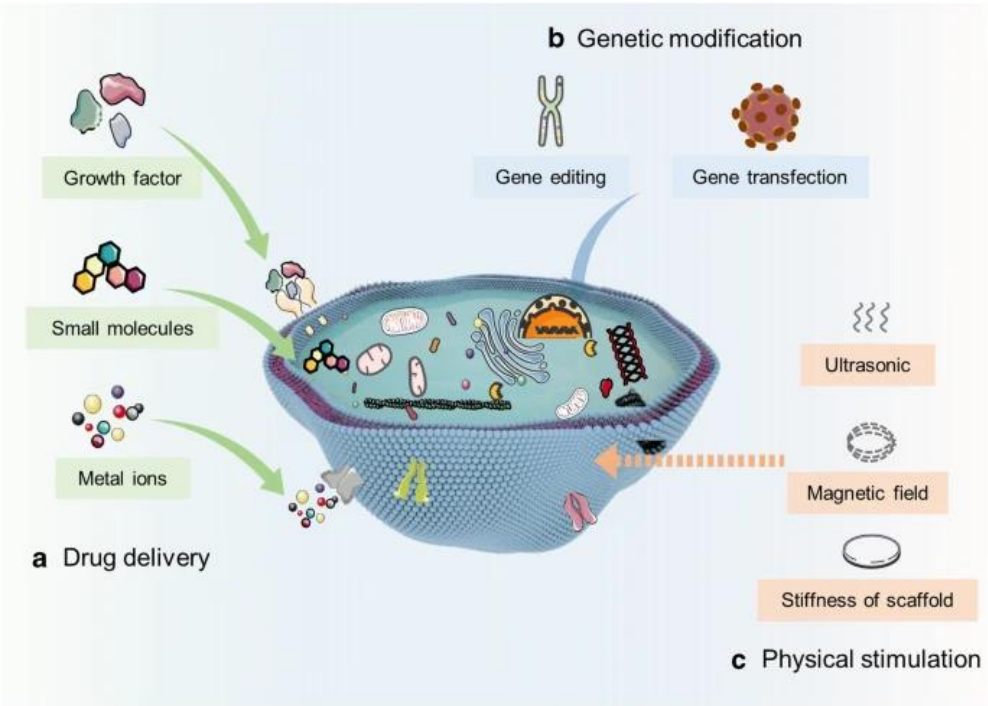
Source Title	ScienceDirect
Source citation (APA Format)	Alinda, S. D., Margono, A., Yulianto, I., Maharti, I. D., & Rafmawan, R. A. (2024). The potential of exosomes from adipose-derived stromal-vascular fraction in Increasing Migration Activity of Human Dental Pulp Stromal Cells (in vitro study). *The Saudi Dental Journal*. https://doi.org/10.1016/j.sdentj.2024.08.005
Original URL	https://www.sciencedirect.com/science/article/pii/S1013905224002359
Source type	Scientific Journal
Keywords	Exosomes, dental pulp stromal cells
#Tags	#DentalPulpRegneration #Exosomes
Summary of key points + notes (include methodology)	As a response to injury in the dental pulp, DPSCs begin to migrate to the area, a process which is heavily dependent on microenvironmental signals. Exosomes have been found to carry and maintain bioactive proteins that help with cell communication which can enhance the DPSC migration, and the researchers have found that AD-SVF is a good source of exosomes. The researchers isolated the AD-SVF using size exclusion chromatography (SEC) and characterized it by using flow cytometry assays and Nanoparticle Tracking Analysis (NTA). The hDPSCs were exposed to the AD-SVF and cultivated until 80% confluence and third to fourth passage by using a control of 0% exposure and two experimental quantities of 0.1% and 1% AD-SVF exposure, and measured at intervals of 6, 24, and 48 hours. The data was analyzed using the Friedman ($p < 0.001$) and Kruskal Wallis ($p < 0.05$) test, and it was found that the wound area decreased after being exposed to the 0.1% and 1% AD-SVF Exo, showing that the hDPSC migration increased as a result of the applied AD-SVF Exo, with the highest result being found at 0.1% exposure.
Research Question/Problem/ Need	How is hDPSC migration affected by AD-SVF Exo?

Important Figures	 Results of the hDPSCs during third and fourth passages compared with after 24-hour starvation
VOCAB: (w/definition)	Adipose-derived – derived from body fat (adipose tissue) Stromal-vascular fraction – a mixture of stromal cells (supportive cells that provide structure to the tissue) and vascular cells (cells related to blood vessels)
Cited references to follow up on	https://www.sciencedirect.com/science/article/pii/S1013905224002359#bb0045\ https://www.scopus.com/record/display.uri?eid=2-s2.0-84881393746&origin=inward&txGid=ddf15e3ff3496c57e0e84ee00ef789e7
Follow up Questions	What are the potential safety and efficacy concerns when using exosomes derived from AD-SVF in clinical applications?

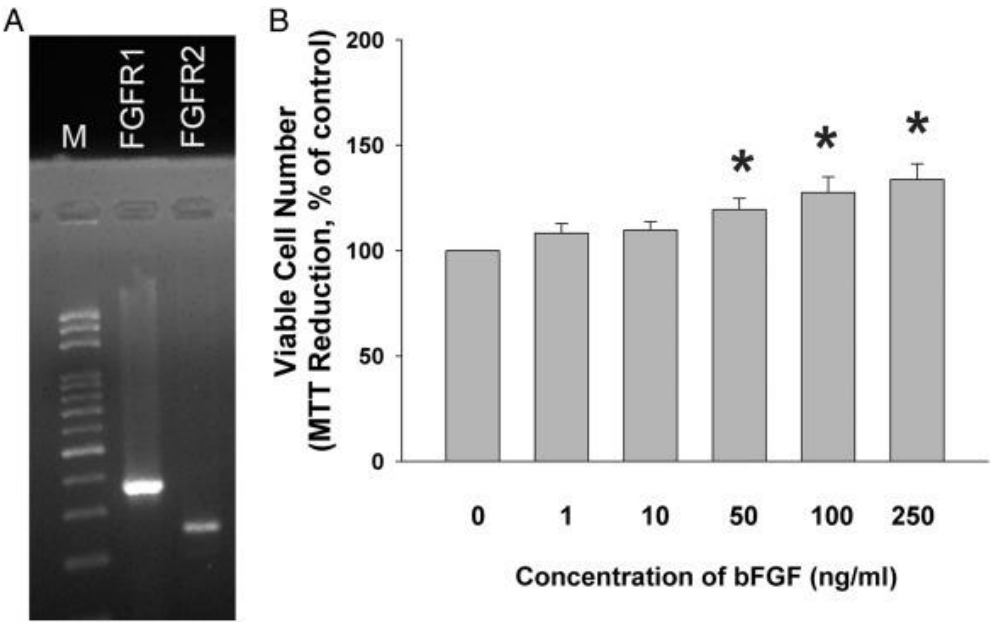
Article #6 Notes: Stem Cell-based Dental Pulp Regeneration: Insights From Signaling Pathways

Source Title	Springer Link
Source citation (APA Format)	Liang, C., Liao, L., & Tian, W. (2021). Stem Cell-based dental pulp regeneration: Insights from signaling pathways. *Stem Cell Reviews and Reports, 17*(4), 1251–1263. https://doi.org/10.1007/s12015-020-10117-3
Original URL	https://link.springer.com/article/10.1007/s12015-020-10117-3
Source type	Science Journal
Keywords	Signaling pathways, dental pulp regeneration, stem cells
#Tags	#DentalPulpRegeneration #SignallingPathways
Summary of key points + notes (include methodology)	The research paper aimed to explore signaling pathways that regulate dental stem cell regeneration. In order to explore the different pathways, researchers used three different methods – drug delivery, genetic modification, and physical stimulation. They found that key cytokines and growth factors are important in migration and proliferation of stem cells and odontogenic differentiation. They also found that transplanting dental stem cells with growth factors can help regenerate vascularized pulp-like tissues.
Research Question/Problem/ Need	How can growth factors help dental stem cells regenerate tooth pulp?
Important Figures	 Graphical abstract

	 Different methods of reactivating signalling transduction
VOCAB: (w/definition)	Growth factors – proteins that help control how cells grow and develop
Cited references to follow up on	Chang, Y. C., et al. (2017). Basic fibroblast growth factor regulates gene and protein expression related to proliferation, differentiation, and matrix production of human dental pulp cells. Journal of Endodontia, 43(6), 936–942. https://doi.org/10.1016/j.joen.2017.01.024.
Follow up Questions	How might patient-specific factors (like age, overall health, or dental history) affect the effectiveness of the regenerative therapies used in the research?

Article #7 Notes: Basic Fibroblast Growth Factor Regulates Gene and Protein Expression Related to Proliferation, Differentiation, and Matrix Production of Human Dental Pulp Cells

Source Title	ScienceDirect
Source citation (APA Format)	Chang, Y.-C., Chang, M.-C., Chen, Y.-J., Liou, J.-U., Chang, H.-H., Huang, W.-L., Liau, W.-C., Chan, C.-P., Jeng, P.-Y., & Jeng, J.-H. (2017). Basic Fibroblast Growth Factor Regulates Gene and Protein Expression Related to Proliferation, Differentiation, and Matrix Production of Human Dental Pulp Cells. *Journal of Endodontics, 43*(6), 936–942. https://doi.org/10.1016/j.joen.2017.01.024
Original URL	https://www.sciencedirect.com/science/article/pii/S0099239917300730?casa_token=-Tt2I_UYE2oAAAAA:apZarzMdHJS2aLEW9GrheSG2GjE_tfISwognFjLnb0QIv9Ux07be0bcdK3B_RX3T7mDvEerTQg
Source type	Journal Article
Keywords	hDPSCs, Basic fibroblast growth factor (bFGF), signalling pathway
#Tags	#SignallingPathway #hDPSCs #bFGFs
Summary of key points + notes (include methodology)	The researchers investigated how basic fibroblast growth factors play a role in cell proliferation, differentiation, and extracellular matrix turnover of dental pulp stem cells. They also explored their involvement in the MEK/ERK signaling pathway. HDPSCs were cultured and studied for FGFR expression using RT-PCR. Cell proliferation was measured using MTT assay, and differentiation was assessed using alkaline phosphatase (ALP) activity. The researchers found that the hDPSCs express both FGFR1 and FGFR2, with bFGF helping cell viability at specific concentrations but reducing ALP activity at higher doses. This means that bFGF can help in dental pulp cell regeneration.
Research Question/Problem/ Need	How can bFGFs help with dental pulp regeneration?

Important Figures	
VOCAB: (w/definition)	Basic fibroblast growth factor – a growth factor that helps with cell growth and tissue repair.
Cited references to follow up on	https://www.nature.com/articles/nrm3528
Follow up Questions	How can environmental factors (like infection) affect bFGF's function in dental pulps?

Article #8 Notes: Wnt signaling activation: targets and therapeutic opportunities for stem cell therapy and regenerative medicine

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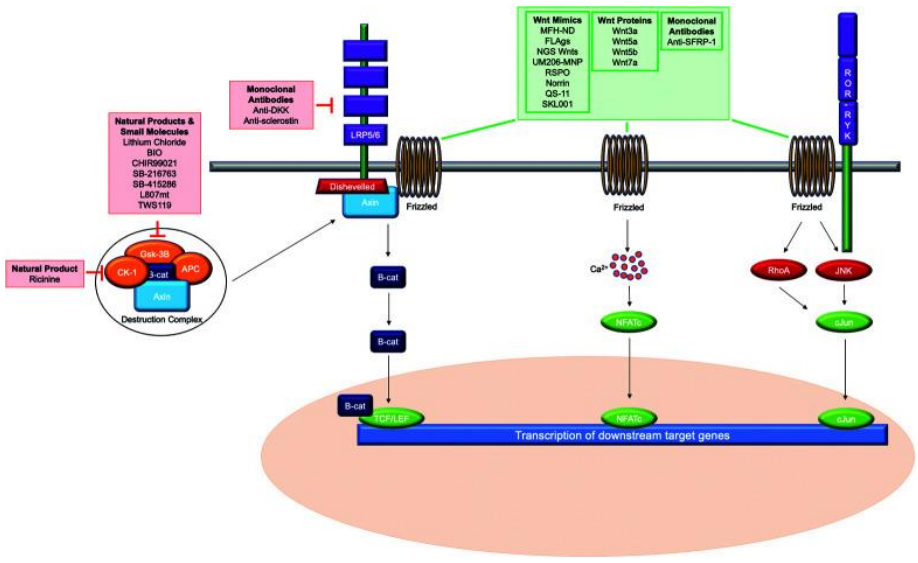
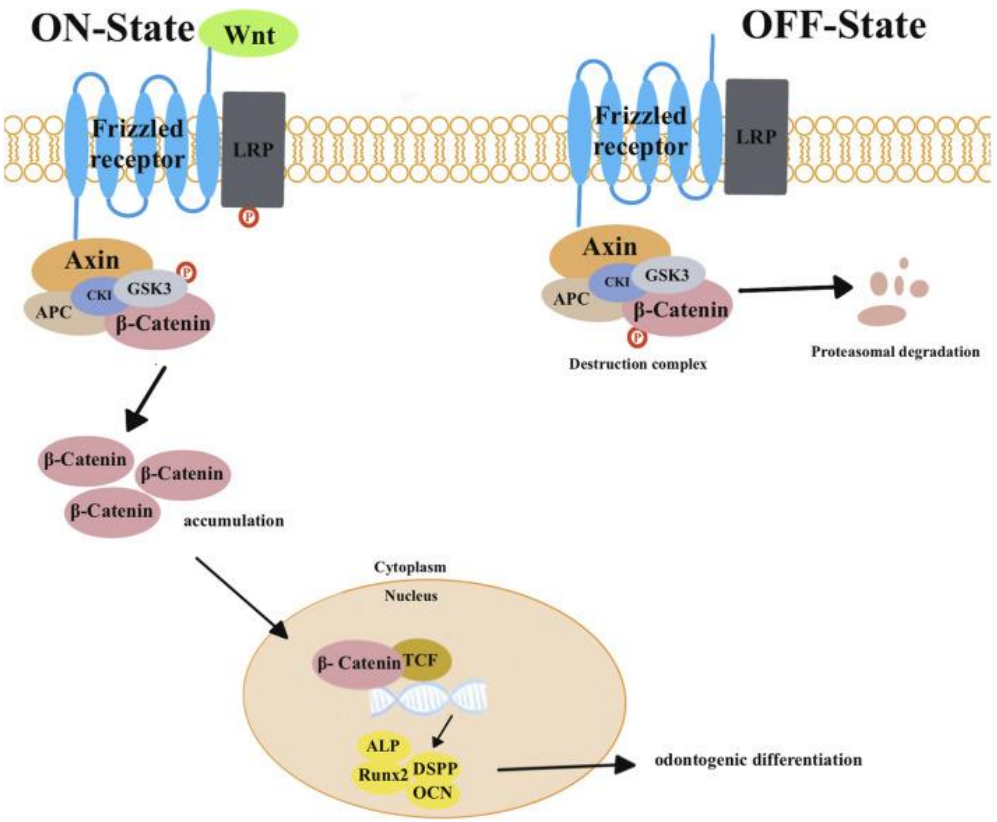
Source Title	National Library of Medicine
Source citation (APA Format)	Bonnet, C., Brahmbhatt, A., Deng, S. X., & Zheng, J. J. (2021). Wnt signaling activation: targets and therapeutic opportunities for stem cell therapy and regenerative medicine. *RSC Chemical Biology, 2*(4), 1144–1157. https://dx.doi.org/10.1039/d1cb00063b.
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8341040/
Source type	Journal Article
Keywords	Wnt signalling, regeneration, stem cell therapy
#Tags	#WntSignallingPathway
Summary of key points + notes (include methodology)	Researchers are interested in the applications of activating and inhibiting the Wnt signalling pathway to help with regeneration as well as to help fight cancer. Wnt is a group of proteins that are responsible for cell communication by helping cells grow, divide, and function. The researchers tested different materials to see what triggers and what inhibits Wnt. The methods they used were high throughput screening, luciferase reporter assays, in vitro and in vivo models, and structural and genetic studies. A high throughput screening is a test that tests large libraries of compounds to see what inhibits and what activates a signalling pathway. A luciferase reporter assay is an assay that measures the activity of Wnt/β-catenin signaling by quantifying luminescence from reporter genes activated by β-catenin. The in vitro and in vivo models tested the biological effects of Wnt modulators, the structural studies used crystallography to see how Wnt antagonists react with their receptors, and the genetic studies investigated the genetic mechanisms regulating Wnt signaling and its modulators. They also used a TOPFlash assay, which measured the Wnt/β-catenin signaling activity. The researchers used activation strategies like monoclonal antibodies, **R-Spondin proteins** (which probably have applications in regenerative medicine), and small molecule inhibitors, like SFRP-1 Inhibitors (which helps with bone formation) and NOTUM Inhibitors (which may help with treating osteoporosis).
Research Question/Problem/ Need	What different materials can inhibit or activate the Wnt signalling pathway and why?

Important Figures	 "Overview of the Wnt signaling pathway and targets of Wnt activators."
VOCAB: (w/definition)	High throughput screening – a test that tests large libraries of compounds to see what inhibits and what activates a signalling pathway. R-Spondin proteins – secreted proteins that enhance the signalling of the Wnt pathway. They help with stem cell regulation and tissue homeostasis.
Cited references to follow up on	https://www.embopress.org/doi/full/10.1038/embor.2011.175 https://www.pnas.org/doi/full/10.1073/pnas.1106083108
Follow up Questions	How can R-Spondin proteins be used to activate Wnt signalling pathway without causing cancer (as in, only by aiding cell regeneration)?

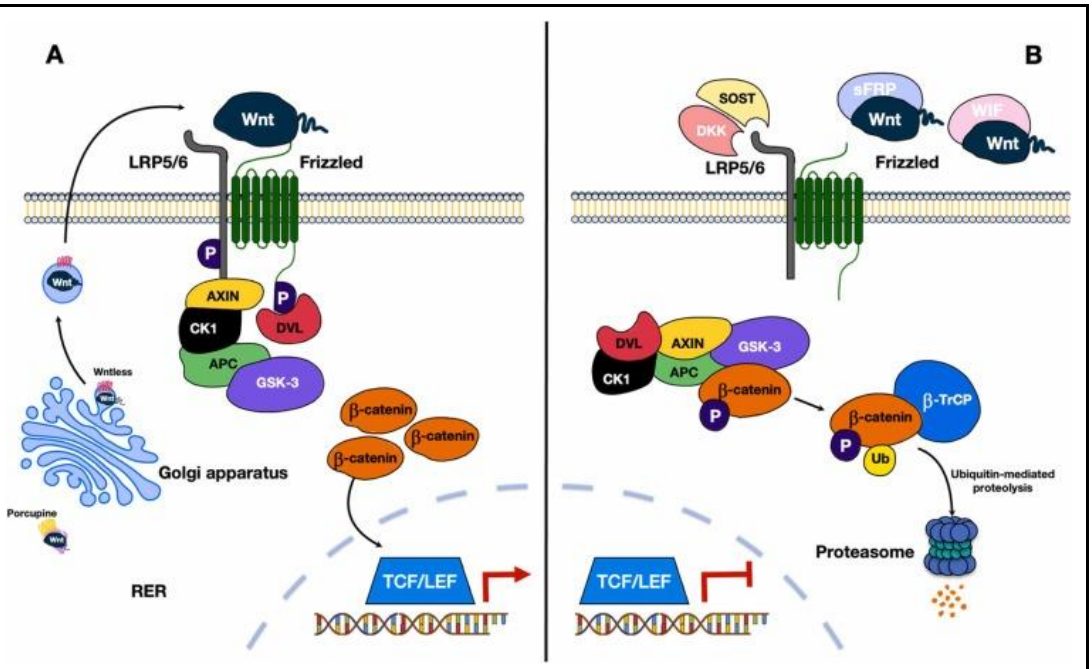
Article #9 Notes: Effects of different signaling pathways on odontogenic differentiation of dental pulp stem cells: a review

Source Title	National Library of Medicine
Source citation (APA Format)	Zhou, L., Zhao, S., Xing, X. (2023) Effects of different signaling pathways on odontogenic differentiation of dental pulp stem cells: a review. *Frontiers in Physiology, 14*. https://doi.org/10.3389/fphys.2023.1272764.
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10622672/
Source type	Journal Article
Keywords	Wnt signalling pathways, DPSCs
#Tags	#WntSignallingPathway #SignallingPathways
Summary of key points + notes (include methodology)	The researchers tested different types of signalling pathways to see their effects on odontogenic differentiation. The canonical pathways of the Wnt signalling pathway involved β-catenin activation for odontogenic differentiation. The non-canonical pathways, such as PCP and Wnt/Ca2+, functioned independently of β-catenin. There have been mixed effects on odontogenic differentiation, though, with some studies showing that β-catenin enhances differentiation and expression of proteins like Runx2, while others show that it inhibits the process. Wild-type SATB2 helps the odontogenic differentiation via Wnt/β-catenin signaling, whereas overexpression of Wnt10A and certain Wnt proteins can suppress it. The BMP/Smad signaling pathways help facilitate the expression of genes like DSPP, DMP-1, ALP, and OCN, and inhibiting these expressions can lead to tooth development disorders and harm dentin regeneration. Studies show that factors like leptin and epiregulin promote the odontogenic differentiation of dental pulp stem cells (DPSCs) by activating the MAPK signalling pathways, which leads to increased expression of differentiation markers such as ALP, DSPP, and Runx2. The NF-kB signalling pathways help with cell proliferation and immune responses, and estrogen deficiency can impair their effects on DPSC differentiation while inhibiting the pathway can increase the differentiation potential. The PI3K/AKT/mTOR signalling pathways are important for cell growth and metabolism, with activated AKT promoting cell survival and differentiation, and inhibiting these pathways can also increase the differentiation potential of DPSCs. The Notch signalling pathway regulates cell differentiation through the interactions between Notch receptors and ligands, with different effects on DPSCs.
Research Question/Problem/ Need	How do different signalling pathways affect odontogenic differentiation of DPSCs?

Important Figures	 Wnt signalling pathway process
VOCAB: (w/definition)	Odontogenic differentiation – the process in which stem cells develop into more specialized cells to form dental structures, like dentin.
Cited references to follow up on	https://stemcellres.biomedcentral.com/articles/10.1186/s13287-021-02660-8
Follow up Questions	Which specific Wnt ligands and receptors are the most important in helping promote odontogenic differentiation in DPSCs and how do they interact with other signalling pathways?

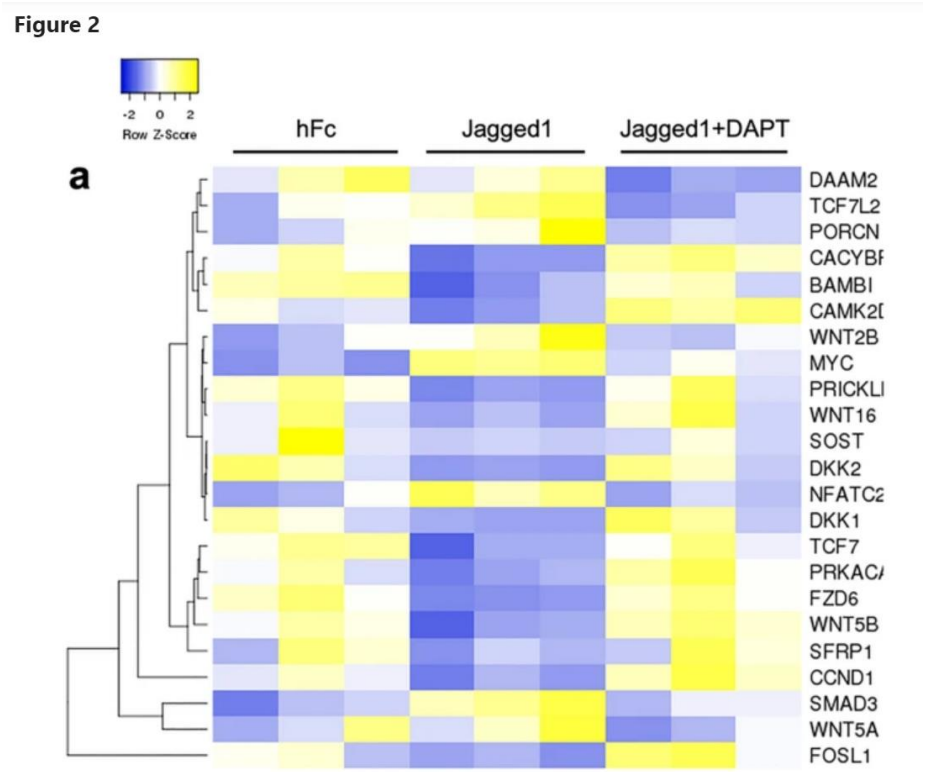
Article #10 Notes: Wnt signaling in dental pulp homeostasis and dentin regeneration

Source Title	ScienceDirect
Source citation (APA Format)	Kornsuthisopon, C., Photichailert, S., Nowwarote, N., Tompkins, K. A., & Osathanon, T. (2022). Wnt signaling in dental pulp homeostasis and dentin regeneration. *Archives of Oral Biology, 134.* https://doi.org/10.1016/j.archoralbio.2021.105322
Original URL	https://www.sciencedirect.com/science/article/abs/pii/S0003996921002855?via%3Dihub
Source type	Journal Article
Keywords	Dentin repair, Wnt Signalling
#Tags	#WntSignalling, #DentalPulpRegeneration
Summary of key points + notes (include methodology)	Wnt proteins act as ligands in the Wnt signalling pathway. Receptors like Frizzled and low-density lipoprotein receptors (LRP) help carry out signal transduction, and there are several activators and inhibitors that modulate that signalling. In the canonical pathway Wnt ligands activate receptors and stabilize β-catenin, which then moves to the nucleus to start gene expression related to Wnt signalling. Non-canonical pathways, on the other hand, operate independently of β-catenin and help with processes like calcium signalling and planar cell polarity, which influences cellular that are important for development. Tooth development depends on the interactions between dental epithelium and mesenchyme. Wnt signalling plays an important role in various stages of this process, including in the tooth initiation and cell differentiation. Experiments show that mice with stabilized β-catenin produce more dentin, although the dentin had a different structure, which proves that excessive Wnt signalling can lead to increased dentin production. The Wnt pathway also affects the epigenetic regulation of dental pulp stem cells through mechanisms like DNA methylation and histone modification.
Research Question/Problem / Need	How does the Wnt Signalling pathway affect dental pulp regeneration? (Review of current knowledge)

Important Figures	 Canonical Wnt signalling pathway
VOCAB: (w/definition)	Frizzled – Receptor that receives signals from Wnt proteins
Cited references to follow up on	https://www.mdpi.com/2073-4409/9/3/652 https://www.jendodon.com/article/S0099-2399(19)30548-5/abstract
Follow up Questions	Why does Wnt signalling increase dentin production, and why does the dentin that is produced by the increase have a different structure than normal dentin?

Article #11 Notes: Non-canonical Wnt signaling participates in Jagged1-induced osteo/odontogenic differentiation in human dental pulp stem cells

Source Title	Scientific Reports
Source citation (APA Format)	Kornsuthisopon, C., Chansaenroj, A., Manokawinchoke, J., Tompkins, K. A., Pirarat, N., & Osathanon, T. (2022). Non-canonical Wnt signaling participates in Jagged1-induced osteo/odontogenic differentiation in human dental pulp stem cells. *Science Reports, 12*. https://doi.org/10.1038/s41598-022-11596-9
Original URL	https://www.nature.com/articles/s41598-022-11596-9
Source type	Journal article
Keywords	Jagged1, Non-canonical Wnt signalling pathway, osteo/odontogenic differentiation
#Tags	#Non-CanonicalWntSignalling #DentalPulpRegeneration #NotchSignalling
Summary of key points + notes (include methodology)	Immobilized Jagged1 proteins were used to seed hDPSCs, which were then maintained in osteo/odontogenic medium for 3, 7, and 14 days. Significantly enhanced mineral deposition was noted after Jagged1 was used to treat the tooth, which proves that activating the Notch signalling pathway can promote osteo/odontogenic differentiation of hDPSCs in vitro. It was also found that DAPT effectively inhibited Notch signalling. The treatment to a tooth by non-canonical Wnt protein, Wnt5A, promoted mineralization.
Research Question/Problem/ Need	How does Wnt signalling help with osteo/odontogenic differentiation in hDPSCs?

Important Figures	Figure 2 
VOCAB: (w/definition)	Jagged1 – a protein in the Notch signalling pathway
Cited references to follow up on	Wnt signaling in development and tissue homeostasis | Development | The Company of Biologists
Follow up Questions	What specific properties of Jagged1 proteins make them useful in osteo/odontogenic differentiation?

Article #12 Notes: An insight into planarian regeneration

Source Title	Wiley Online Library
Source citation (APA Format)	Ge, X., Han, X., Zhao, Y., Cui, G., & Yang, Y. (2022). An insight into planarian regeneration. *Cell Proliferation, 55*(9). https://doi.org/10.1111/cpr.13276
Original URL	https://onlinelibrary.wiley.com/doi/10.1111/cpr.13276
Source type	Review Journal Article
Keywords	Planaria, Wnt Signalling
#Tags	#Planaria #WntPlanaria
Summary of key points + notes (include methodology)	The regenerative properties of planaria are mostly due to neoblasts. Planarian stem cells are regarded as heterogeneous cells characterized by a high ratio of nucleus to cytoplasm. After injury, over 200 genes are activated, but the missing-tissue response (MTR) is specifically induced only by tissue loss, such as during amputation. The gene Smed-follistatin has been identified as crucial for MTR, as it regulates regeneration speed and is only expressed in response to injury, not during homeostasis. Blocking follistatin prevents successful regeneration and disrupts the re-establishment of the anterior-posterior (A/P) axis by negatively regulating Wnt signaling, which is vital for head regeneration. Wnt helps with head regeneration, so inhibiting Wnt signalling after an amputation can result in the regeneration of tails in the wrong places. Disruption of bioelectric networks can cause permanent morphological abnormalities.
Research Question/Problem/ Need	What is currently known about planarian regeneration?
Important Figures	
VOCAB: (w/definition)	Neoblasts – a stem cell found in flatworms that can divide to create almost any cell type in the worm's body Smed-follistatin (fst) gene – a gene that plays a role in tissue regeneration in planaria
Cited references to follow up on	https://pubmed.ncbi.nlm.nih.gov/19686688/
Follow up Questions	In what ways do bioelectric signals modulate Wnt signaling during the early stages of regeneration?

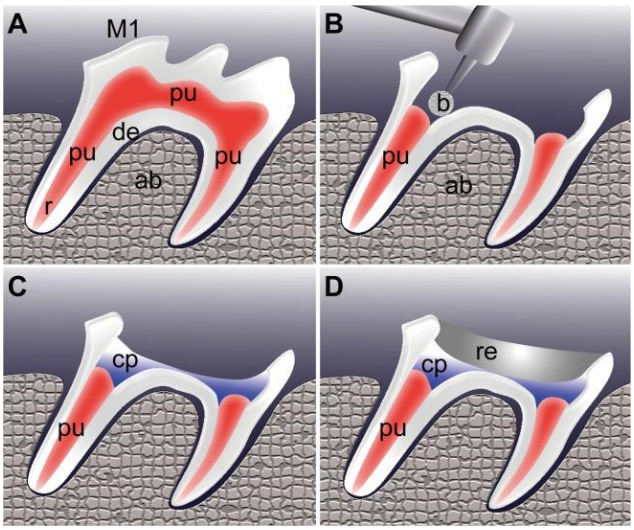
Article #13 Notes: Wnt signaling in planarians: new answers to old questions

Source Title	The International Journal of Developmental Biology
Source citation (APA Format)	Almuedo-Castillo, M., Sureda-Gómez, M., & Adell, T. (2012). Wnt signaling in Planarians: New answers to old questions. *The International Journal of Developmental Biology, 56*(1-2–3), 53–65. https://doi.org/10.1387/ijdb.113451ma
Original URL	https://ijdb.ehu.eus/article/113451ma
Source type	Journal Article
Keywords	Planaria, Wnt1, RNAi
#Tags	#Planaria #WntSignallingPathway
Summary of key points + notes (include methodology)	Wnt signalling pathway split (like canonical vs. non-canonical due to b-catenin involvement) is sort of artificial but can be useful in context-specific result. Schmidtea mediterranea is valuable in studying Wnt because of their regenerative abilities. Wnt genes show distinct expression regions – for example, wnt1 is localized in the posterior dorsal midline, while wnt11-1 and wnt11-2 are expressed in the tail. Silencing Wnt genes through RNA interference (RNAi) produces many different phenotypes. Wnt1, when silenced, can lead to “two-headed” or “tailless” phenotypes, indicating its role in canonical Wnt signaling. Wnt11-2 also contributes to tail morphology but does not affect polarity reversal. Wnt1 is the first to express after amputation, and its response is free of stem cells. The interaction among Wnt ligands is crucial for proper AP patterning. It is proposed that wnt1 and wnt11-5 work together through β-catenin to control posterior identity. The Hedgehog (Hh) signaling pathway may also influence Wnt activation during regeneration, with evidence suggesting Hh acts upstream of β-catenin. The planarian homolog of Notum, a secreted hydrolase, is crucial for establishing anterior-posterior (AP) polarity. It is upregulated at anterior wounds shortly after amputation and inhibits posterior specification. Silencing notum leads to “two-tailed” planarians. A coherent model for early AP fate decisions suggests that wnt1 activation leads to β-catenin-1 activation and subsequently influences genes like wnt11-5 and notum. In anterior wounds, Notum and sFRP-1 inhibit Wnt signaling to facilitate head differentiation, while in posterior wounds, wnt1 is maintained, activating additional downstream targets. Wnt5, the only described non-canonical Wnt in planarians, is implicated in controlling neural connectivity and limiting the growth of the nervous system along the medio-lateral axis.
Research Question/Problem/	How do Wnt signalling pathways influence axial polarity and cell fate

Need	decisions during the regeneration of Schmidtea mediterranea?
Important Figures	
VOCAB: (w/definition)	Axial polarity – the ordered distribution of structures along an axis
Cited references to follow up on	
Follow up Questions	How do Wnt5 and Slit interact and influence each other's expression during nervous system regeneration in schmidtea mediterranea?

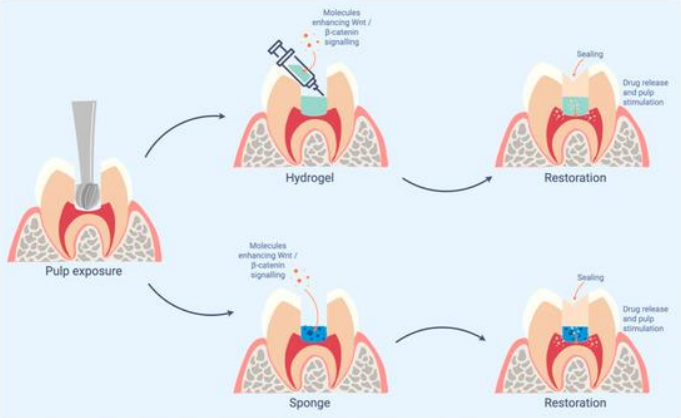
Article #14 Notes: Topical Application of Lithium Chloride on the Pulp Induces Dentin Regeneration

Source Title	PLOS ONE
Source citation (APA Format)	Ishimoto, K., Hayano, S., Yanagita, T., Kurosaka, H., Kawanabe, N., Itoh, S., Ono, M., Kuboki, T., Kamioka, H., & Yamashiro, T. (2015). Topical application of lithium chloride on the pulp induces dentin regeneration. *PLOS ONE, 10*(3). https://doi.org/10.1371/journal.pone.0121938
Original URL	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0121938
Source type	Journal Article
Keywords	Lithium chloride, dentin regeneration, transdifferentiation, topical agent
#Tags	#LiCl #WntSignalling #DentinRegeneration #Methodology
Summary of key points + notes (include methodology)	The researchers focused on activitating the canonical Wnt signalling pathway to trigger the natural process of dentinogenesis. The removed the coronal (or crown) and pulp of the molar and applied the activator lithium chloride. The goal was to encourage transdifferentiation towards odontoblasts from the surrounding pulpal cells. MicroCT proved that LiCl succeeded in inducing dentin repair and even the formation of a dentin bridge. They tested on mice and applied LiCl as a topical agent by mixing it material carriers (macrogol and propylene glycol in a 1:1 ratio) to achieve a concentration of 10 mM LiCl. The cavity was then coated with a bonding agent and cured for 20 seconds. Three-dimensional images of the tooth structure were obtained using a Microfocus X-ray CT system at specific voltage and current settings. The images were reconstructed at a spatial resolution of 17 µm and processed with VG Studio MAX 2.0 software. Teeth and surrounding bone were fixed in 4% paraformaldehyde overnight, decalcified in 12.5% EDTA for three weeks, dehydrated, embedded in paraffin, and sectioned at 7 µm for hematoxylin and eosin staining. Frozen sections (10 µm) were also prepared for in situ hybridization. Digoxigenin-labeled RNA probes were used for in situ hybridization to detect gene expression, with the preparation of Dspp RNA probes referenced from previous studies. Quantitative comparisons were made using the Mann-Whitney U test, with significance defined at $p < 0.05$.
Research Question/Problem/ Need	How can lithium chloride be used in vivo to help aid in Wnt-induced dentin regeneration?

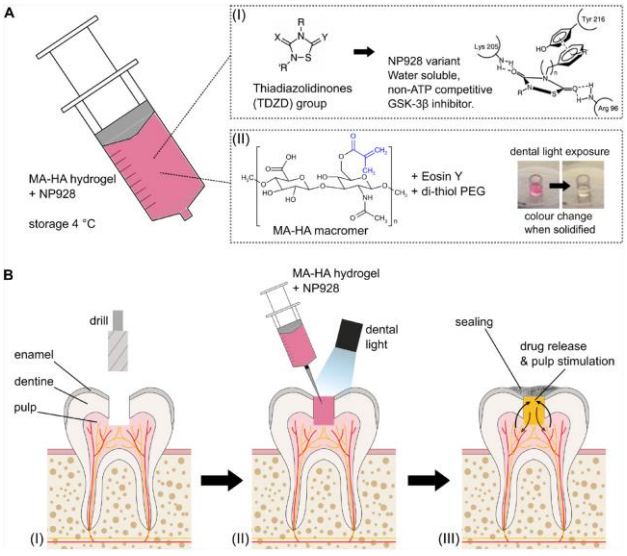
Important Figures	 graphical description of process
VOCAB: (w/definition)	Transdifferentiation – the process where one type of cell transforms into another type without first becoming a stem cell.
Cited references to follow up on	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0121938
Follow up Questions	What properties in LiCl help with activating the Wnt signalling pathway and why?

Article #15 Notes: Modulators of Wnt Signaling Pathway Implied in Dentin Pulp Complex Engineering: A Literature Review

Source Title	MDPI Open Access Journals
Source citation (APA Format)	Florimond, M., Minic, S., Sharpe, P., Chaussain, C., Renard, E., & Boukpessi, T. (2022). Modulators of Wnt Signaling Pathway Implied in Dentin Pulp Complex Engineering: A Literature Review. *International Journal of Molecular Sciences, 23*(18). https://doi.org/10.3390/ijms231810582
Original URL	https://www.mdpi.com/1422-0067/23/18/10582
Source type	Review Journal Article
Keywords	NP928, Wedelolactone, Wnt Signalling, Activators
#Tags	#WntSignalling #Planaria #NP928 #Wedelolactone #Methodology
Summary of key points + notes (include methodology)	Dental caries leading to pulp exposure is treated with inorganic calcium-containing materials like calcium hydroxide (CH), mineral trioxide aggregate (MTA), and Biodentine, which help in forming new dentin from odontoblast-like cells derived from resident stem cells in the pulp. GSK3 inhibitors can help improve reparative dentin formation. Tideglusib is a well-studied GSK3 inhibitor that upregulates Wnt activity and promotes dentin regeneration but has low solubility, and so **NP928** is a modified version of it. Tivantinib, another small molecule, inhibits GSK3 and has low toxicity in dental pulp cells, but requires further investigation in vivo. Lithium chloride (LiCl) also inhibits GSK3 and has been shown to stimulate reparative dentin formation. R-spondin 2 is a Wnt agonist that enhances odontogenic differentiation in dental pulp stem cells (DPSCs) by activating Wnt/β-catenin signaling, increasing expression of key odontogenic markers. **Wedelolactone** is a natural compound that helps promote odontoblast differentiation and mineralisation in DPSCs by enhancing β-catenin nuclear accumulation and expression of odontoblast-related genes.
Research Question/Problem/ Need	What modulators can help activate the Wnt signalling pathway to help with dental pulp regeneration?

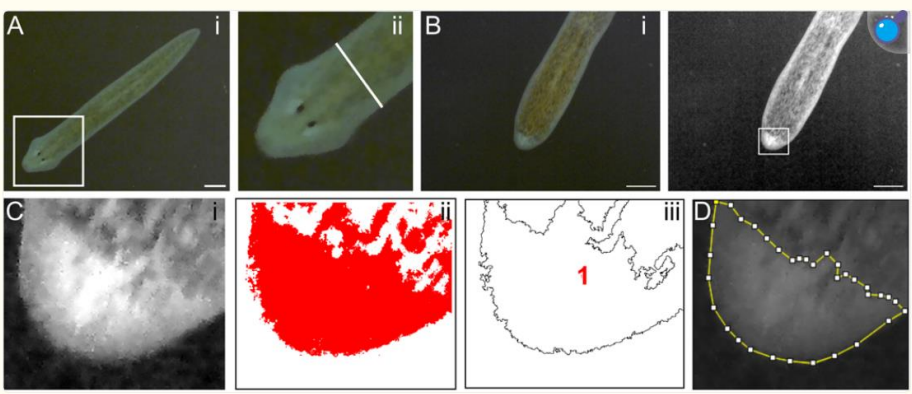
Important Figures	
VOCAB: (w/definition)	
Cited references to follow up on	https://www.liebertpub.com/doi/10.1089/cell.2018.0004
Follow up Questions	How do NP928 and Wedelolactone help with dental pulp regeneration? What do they have in common with LiCl?

Article #16 Notes: GSK3 Inhibitor-Induced Dentinogenesis Using a Hydrogel

Source Title	Sage Journals
Source citation (APA Format)	Alaohali, A., Salzlechner, C., Zaugg, L. K., Suzano, F., Martinez, A., Gentleman, E., & Sharpe, P. T. (2021). GSK3 inhibitor-induced dentinogenesis using a hydrogel. *Journal of Dental Research, 101*(1), 46–53. https://doi.org/10.1177/00220345211020652
Original URL	https://journals.sagepub.com/doi/10.1177/00220345211020652
Source type	Journal Article
Keywords	Hydrogel, NP928
#Tags	#NP928 #Methodology #DentinRegeneration #WntSignalling
Summary of key points + notes (include methodology)	Researchers developed a small-molecule drug that targets GSK3 to inhibit it and stimulate reparative dentine formation. This drug belongs to thiadiazolidinone (TDZD) family of drugs and has similar properties to tideglusib, but unlike the other drugs of the family, NP928 is more water soluble and thus can be directly delivered to pulp lesions. It can be part of a biodegradable hydrogel (Methacrylate (MA)–hyaluronic acid (HA) hydrogel) and can be placed onto the tooth by syringe. Media was treated with NP928
Research Question/Problem/ Need	How can tideglusib be improved to become more water soluble and thus easily appliable to the tooth?
Important Figures	 Shows how NP928 can be used on the tooth
VOCAB:	Dentinogenesis – the formation of dentin from odontoblasts

(w/definition)	
Cited references to follow up on	https://pubs.acs.org/doi/full/10.1021/jm011020u?casa_token=g8J9Zv7T4KgAAAAA%3AEXPMyeG9C7-lb8IRBoeW6JvBT0r8EOde52CB5TL93NLzV5gmWyAbxYbBqpor9rG9PuGjyPvyVC8CCf_m
Follow up Questions	

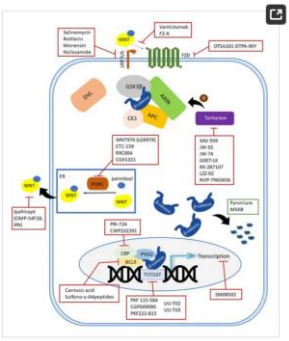
Article #17 Notes: A Simple Method for Quantifying Blastema Growth in Regenerating Planarians

Source Title	American Association for Anatomy
Source citation (APA Format)	Campillo, N., Ireland, D., Patel, Y., & Collins, E. S. (2023a). A simple method for quantifying blastema growth in regenerating planarians. *Current Protocols, 3*(3). https://doi.org/10.1002/cpz1.684
Original URL	https://currentprotocols.onlinelibrary.wiley.com/doi/10.1002/cpz1.684
Source type	Journal Article
Keywords	Planaria, Fiji/ImageJ
#Tags	#Planaria #Methodology
Summary of key points + notes (include methodology)	The article describes different protocols for quantifying blastema growth in regenerating freshwater planarians. The methods described in the article discuss the usage of Fiji/ImageJ software to map out the growth of the planaria, using a caliber or other tool with measurements as a "standard" for the software to compare against. The protocols describe a specific plan for how to image the planaria over the course of 2 weeks (Basic Protocol 1), then described the specific steps for quantifying the blastema size (Basic Protocol 2) and calculating the growth rate using a linear curve fitting in a spreadsheet (Basic Protocol 3).
Research Question/Problem/ Need	How can the rate of blastema growth in regenerating planarians be quantified to assess the effects of chemicals on stem cell biology and regeneration?
Important Figures	 Explains how the images help measure blastema growth
VOCAB: (w/definition)	ImageJ/Fiji - software that can help quantify blastema growth of planaria

Cited references to follow up on	Schindelin J, Arganda-Carreras I, Frise E, Kaynig V, Longair M, Pietzsch T, … Cardona A. (2012). Fiji: An open-source platform for biological-image analysis. Nature Methods, 9, 676–682. doi: 10.1038/nmeth.2019
Follow up Questions	How can I get access to this software?

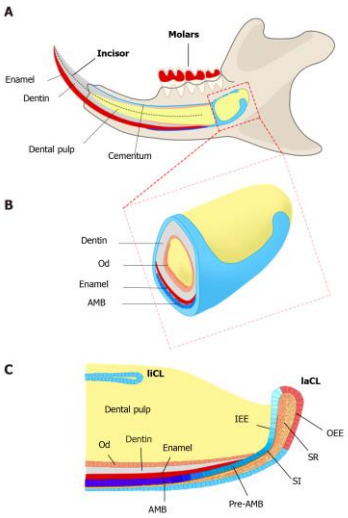
Article #18 Notes: Wnt Signaling Inhibitors and Their Promising Role in Tumor Treatment

Source Title	MDPI
Source citation (APA Format)	Pećina-Šlaus, N., Aničić, S., Bukovac, A., & Kafka, A. (2023). Wnt signaling inhibitors and their promising role in tumor treatment. *International Journal of Molecular Sciences, 24*(7). https://doi.org/10.3390/ijms24076733
Original URL	https://www.mdpi.com/1422-0067/24/7/6733
Source type	Journal Article
Keywords	Wnt signaling pathway; β-catenin; porcupine; Wnt inhibitors; mutations; tumors
#Tags	#WntSignalling #Inhibitor #CanonicalWntSignalling
Summary of key points + notes (include methodology)	The article talks about the usage of different inhibitors to knock out specific components in the Wnt signaling pathway, which can help with tumor treatment. The Wnt pathway is often altered in tumors, leading to its activation that promotes tumor growth. Researchers have found many such inhibitors that target specific components of the Wnt pathway. For example, silencing β-catenin is effective in inhibiting colorectal cancer growth. However, the tumor quickly resumes after stopping treatment, which suggests that continuous therapy would be needed for such a solution. Other strategies have also been shown to help, like inhibiting the β-catenin with TCF and knocking down TCF4. There are still many challenges associated with targeting β-catenin and its binding sites though, because of the difficulty of designing small molecules that can specifically inhibit the nuclear form of β-catenin.
Research Question/Problem/ Need	Can inhibiting the Wnt signaling pathway serve as an effective therapeutic strategy for cancer treatment, and what are the challenges and potential of targeting specific components of this pathway?

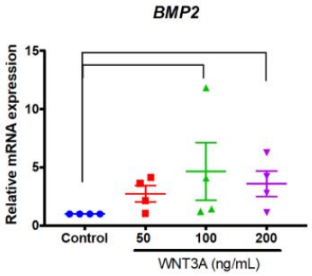
Important Figures	 **Figure 2.** Schematic representation of inhibitors targeting the canonical Wnt components.
VOCAB: (w/definition)	
Cited references to follow up on	Kahn, M. Can we safely target the WNT pathway? Nat. Rev. Drug Discov. 2014, 13, 513–532
Follow up Questions	How does continuous administration of Wnt inhibitors affect tumor progression and patient survival rates?

Article #19 Notes: New insight into dental epithelial stem cells: Identification, regulation, and function in tooth homeostasis and repair

Source Title	Baishideng Publishing Group
Source citation (APA Format)	Gan, L., Liu, Y., Cui, D.-X., Pan, Y., & Wan, M. (2020). New insight into dental epithelial stem cells: Identification, regulation, and function in tooth homeostasis and repair. World Journal of Stem Cells, 12(11), 1327–1340. https://doi.org/10.4252/wjsc.v12.i11.1327
Original URL	https://www.wjgnet.com/1948-0210/full/v12/i11/1327.htm
Source type	Journal Article
Keywords	Dental epithelial stem cells; Tissue engineering; Label-retaining cells; Lineage tracing; Single-cell sequencing
#Tags	#DentalEpithelialStemCells
Summary of key points + notes (include methodology)	The article discusses the regenerative potential of tooth enamel, which is a highly mineralized tissue that makes up the outermost layer of the tooth. This tissue cannot repair itself after caries or trauma damage due to the loss of DESCs and ameloblasts after the tooth erupts. The article explores the identification and regulatory mechanisms of DESCs in mouse incisors, which can grow continuously due to the DESCs present that regenerate enamel-producing ameloblasts. The researchers use methods like label-retaining cells and lineage tracing, showing that DESCs reside in the labial cervical loop, and can regenerate ameloblasts and other dental epithelial lienages.
Research Question/Problem/ Need	How do dental epithelial stem cells (DESCs) in mouse incisors contribute to enamel formation, homeostasis, and repair, and what are the regulatory mechanisms underlying their function?

Important Figures	 the structure and function of dental epithelial stem cells (DESCs) in mouse incisors
VOCAB: (w/definition)	Dental Epithelial Stem Cells – specialized cells in the dental tissue that can self-renew and differentiate into various cell types, such as enamel-producing ameloblasts, to support tooth growth and repair
Cited references to follow up on	Yang G, Zhou J, Teng Y, Xie J, Lin J, Guo X, Gao Y, He M, Yang X, Wang S. Mesenchymal TGF-β signaling orchestrates dental epithelial stem cell homeostasis through Wnt signaling. Stem Cells. 2014;32:2939-2948.
Follow up Questions	What challenges exist in utilizing DESC for enamel tissue engineering?

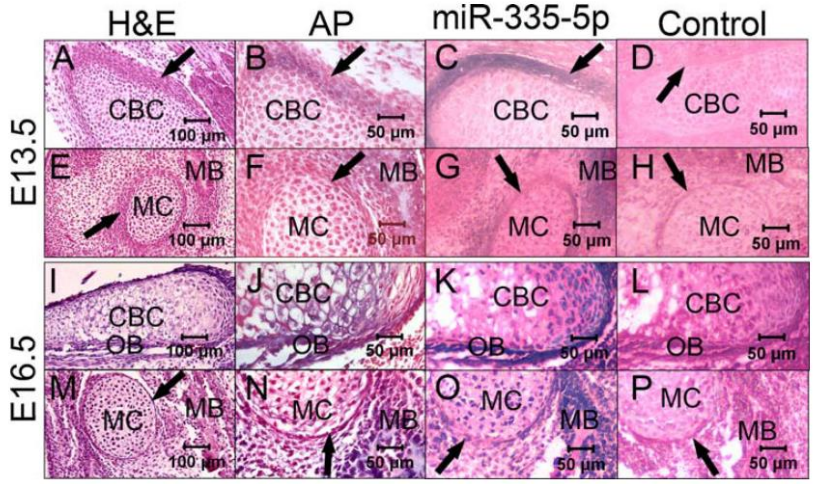
Article #20 Notes: Wnt3a promotes odonto/osteogenic differentiation in vitro and tertiary dentin formation in a rat model

Source Title	Wiley Online Library
Source citation (APA Format)	Sukarawan, W., Rattanawarawipa, P., Yaemkleebbua, K., Nowwarote, N., Pavasant, P., Limjeerajarus, C. N., & Osathanon, T. (2023). WNT3A promotes odonto/osteogenic differentiation *in vitro* and tertiary dentin formation in a rat model. *International Endodontic Journal*, *56*(4), 514–529. https://doi.org/10.1111/iej.13888
Original URL	https://onlinelibrary.wiley.com/doi/10.1111/iej.13888
Source type	Journal Article
Keywords	Wnt3A, dentinogenesis, SHED, odontogenesis
#Tags	#Wnt3A #Activator
Summary of key points + notes (include methodology)	The aim of the researchers of this paper was to investigate the effect of Wnt3A on odonto/osteogenic differentiation of SHEDs and reparative dentine formation in a rat model. SHEDs were cultured with various concentrations of Wnt3A (50–200 ng/ml), showing decreased colony formation and increased expression of osteogenic markers (OSX, BMP2, DMP1) along with enhanced mineralization. Wnt3A treatment led to significant dentine / bone volume formation in rat model with pulp exposure, promoting tertiary dentine formation at the defect sites.
Research Question/Problem/ Need	What is the effect of Wnt3a on the odonto/osteogenic differentiation of stem cells isolated from human exfoliated deciduous teeth (SHEDs), and how does it influence reparative dentine formation in a rat model?
Important Figures	 **FIGURE 8** Wnt3a promoted *BMP2* expression in stem cell from human exfoliated deciduous teeth (SHEDs). Cells were treated with Wnt3a at concentrations of 50, 100, or 200 ng/ml in a normal growth medium for 7 days. *BMP2* mRNA expression was determined using real-time qPCR. Bars indicate a significant difference compared with the control ($p < .05$).

VOCAB: (w/definition)	Wnt3A – protein of the Wnt signalling pathway that shows convincing evidence of aiding in regeneration (by activating the Wnt signalling pathway)
Cited references to follow up on	Cruciat, C.M. & Niehrs, C. (2013) Secreted and transmembrane wnt inhibitors and activators. Cold Spring Harbor Perspectives in Biology, 5(3), a015081.
Follow up Questions	Where could I get access to wnt3a?

Article #21 Notes: Effects of miR-335-5p in Modulating Osteogenic Differentiation by Specifically Downregulating Wnt Antagonist DKK1

Source Title	Journal of Bone and Mineral Research
Source citation (APA Format)	Zhang, J., Tu, Q., Bonewald, L. F., He, X., Stein, G., Lian, J., & Chen, J. (2011). Effects of mir-335-5p in modulating osteogenic differentiation by specifically downregulating Wnt antagonist DKK1. *Journal of Bone and Mineral Research, 26*(8), 1953–1963. https://doi.org/10.1002/jbmr.377
Original URL	https://academic.oup.com/jbmr/article-abstract/26/8/1953/7597920?redirectedFrom=fulltext&login=false
Source type	Journal Article
Keywords	Osteogenic Differentiation, DKK1, Wnt Antagonist
#Tags	#WntSignallingPathway #DKK1 #Differentiation #DentalPulpRegeneration
Summary of key points + notes (include methodology)	The study focused on the usage of miR-335-5p to downregulate DKK1, which is a protein that inhibits the Wnt Signalling pathway and thus induces osteogenic differentiation. This process essentially enhances Wnt signalling, as seen by elevated GSK-3β phosphorylation and increased β-catenin transcriptional activity. The researchers used miRNA microarray analysis, luciferase assays, and in situ hybridization and ATP staining to measure their results. It was found that miR-335-5p helps with osteogenic differentiation.
Research Question/Problem/ Need	How does miR-335-5p aid in osteogenic differentiation?

Important Figures	 In situ hybridization showing in vivo distribution of miR-335-5p in mouse embryos
VOCAB: (w/definition)	mRNA – messenger RNA
Cited references to follow up on	Xiao G, Gopalakrishnan R, Jiang D, Reith E, Benson MD, Franceschi RT. Bone morphogenetic proteins, extracellular matrix, and mitogenactivated protein kinase signaling pathways are required for osteoblast-specific gene expression and differentiation in MC3T3-E1cells. J Bone Miner Res. 2002;17:101–110.
Follow up Questions	How might miR-335-5p and its regulation of DKK1 enhance Wnt pathway activity in odontogenesis?