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REVIEW ARTICLE **OPEN ACCESS**

Parallelism inhallmarks of Cancer and Wound healing

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ABSTRACT:
A variety of mechanisms which drive cancer development and progression also promote wound healing. Tissue repair and cancer share diverse cellular and molecular processes that are regulated in a wound but misregulated in cancer. Tissue repair and cancer also share cellular and molecular processes that are regulated in a wound but misregulated in cancer. There are many parallels viz sustained proliferative signaling, activation of invasion and angiogenesis to the promoting role of inflammation through which one process can inform the other. Human genomic datasets can also provide the means for further exchange of concepts between the cancer and wound healing fields. Utilizing population health approaches in patient datasets will enable the analysis of transcriptomic and epigenetic parallels (and differences) between repairing wounds and the signatures of various cancers at different stages of their progression. All of these insights together will hopefully guide us towards further opportunities for repurposing drugs designed to treat cancer as wound healing therapeutics and vice versa.
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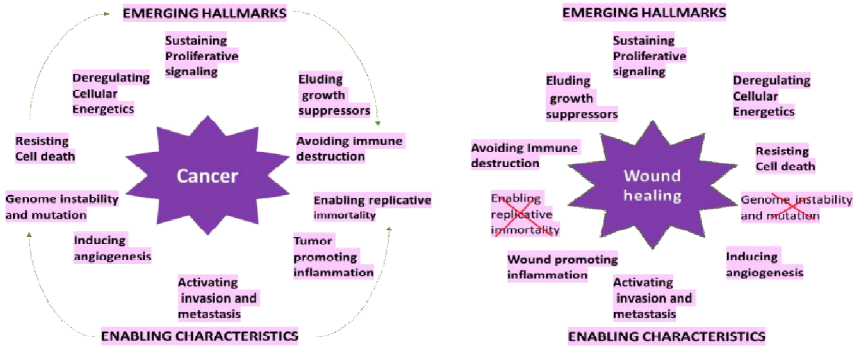
INTRODUCTION

There has existed a long-time association between wound healing and cancer and cancer is often described as a "wound that does not heal". [1]

Tissue repair during wound healing and cancer share cellular and molecular processes that are well regulated in a wound but mis-regulated in cancer. There are many parallels through which one process can inform the other viz sustained proliferative signalling, activation of invasion, angiogenesis and inflammation. For some hallmarks, the parallels are more dubious. It was earlier considered that tumours appear to behave like wounds that fail to heal [2-5]. Laterit became clear that there are multiple shared mechanisms that differ in their regulation during cancer growth and metastasis [6,7].

Acute wound repair normally has a resolution phase whereas tumours behave more like a chronic wound, which has no resolution phase.The genomic datasets and mechanistic findings gathered from studying wound healing may provide us potential insights into the processes that are involved in tumorigenesis and vice versa due to the parallels between both. Hanahan and Weinberg's "Hallmarks of Cancer" papers [8,9] highlight the key mechanisms that appear to underpin all cancers. Many of these "hallmarks" and "enabling characteristics" may also be shared by those mechanisms that underpin healing wounds (Fig. 1).

Fig 1: Hallmarks of Cancer to illustrate parallels between Cancer and wound healing



The necessary and precisely activated mechanism for tissue repair is mirrored by dysregulation in a growing cancer. This helped to understand the parallels and enabling characteristics between these two processes and their research disciplines.

Table 1:HALLMARKS AND ENABLING CHARACTERISTICS WITH THE CLEAREST PARALLELS

HALLMARKS AND ENABLING CHARACTERISTICS WITH THE CLEAREST PARALLELS		
HALLMARKS	**PARALLELS**	**REFERENCE**
1.	Sustaining proliferative signaling	Macheretet al (10)
2.	Activation of invasion (and metastasis)	Martin et al (11)
3.	Tumor and repair-promoting inflammation	Khusnurrokhman et al (12)
4.	Angiogenesis	Majidpoor et al (13)
5.	Resisting cell death	Townsend et al (14)
6.	Avoiding immune cell destruction	Messerschmidt et al (15)
7.	Deregulating cellular energetics	Stine et al (16)
CANCER HALLMARKS THAT MIGHT NOT BE SHARED BY REPAIRING TISSUES		
HALLMARKS	**PARALLELS**	**REFERENCE**
1.	Evading growth suppressors and enabling replicative immortality	Gutschner et al (17)
2.	Genomic instability and mutation	Yao et al (18)
SHARED HALLMARKS THAT ARE NOT BONAFIDE CANCER HALLMARKS (YET)		
HALLMARKS	**PARALLELS**	**REFERENCE**
1.	The microbiome and dysbiosis	Vimal et al (19)
2.	Aberrant matrix deposition	Elgundi et al (20)
3.	Adipocytes: Not silent bystanders	Qi Wu et al (21)

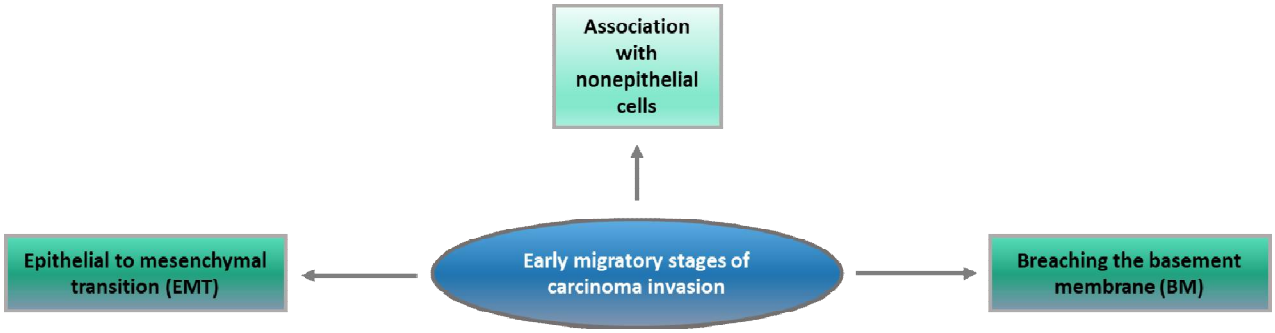
HALLMARK 1: SUSTAINING PROLIFERATIVE SIGNALLING

Constitutive activation of proliferative signalling or failure of normal negative feedback mechanisms can drive uncontrolled cell proliferation in cancer [22]. Incontrast, tissue damage leads to some tissue loss, and generally, these missing cells need to be replaced as a part of the tissue repair process. In a tumor, cell proliferation can appear disorganized and haphazard whereas wounding triggers a coordinated and synchronized proliferative response. [23,24]Proliferation in tumours is caused by constitutive, intrinsic changes in mitogenic signalling but proliferation in wounds is specifically induced by tissue damage and halts when repair is complete. [25,26]

HALLMARK 2: ACTIVATION OF INVASION (AND METASTASIS)

One of the most keenly investigated hallmarksof cancer is that generally cancers kill when they become invasive and metastasize. Re-epithelialization during wound closure bears considerable similarity to processes which occur in the early migratory stages of carcinoma invasion. (Fig 2)

Fig 2: Processes during early migratory stages of carcinoma invasion



Many genes are switched on in the advancing epidermal wound edge cells and form the transcriptional signature(s) of invasive carcinomas [reviewed in (6)].
The invading fronts of a carcinoma usually comprises of small groups of outgrowing cells and the advancing wound epidermal tongue is quite similar as it is also limited to only one or two cell layers at the advancing tip. [27]

HALLMARK 3: TUMOR- AND REPAIR-PROMOTING INFLAMMATION

The early cancer microenvironment resembles a chronic wound [28]. The recruitment of inflammatory cells and their delivery of supportive factors like TGF-βs 1 and 2 and family of growth factors like platelet-derived growth factors (PDGFs) are important for both tumor development and wound healing.[29,30]Prostaglandin E2 (PGE2)isone of the wound-inflammation-induced trophic signals. (1)

HALLMARK 4: ANGIOGENESIS

Folkman lab has studied tumor-derived angiogenic signals and how they might be dampened to block the rate-limiting step i.e. growth of tumours beyond 1 mm in diameter without recruiting their own vascular supply, largely from pre-existing vessels in the vicinity in cancer progression. [31]. Cancer-associated vessels are visibly different from normal tissue vasculature and they tend to be complicated, disorganized and leaky and remain so throughout cancer progression [32].
Wound angiogenesis also initially consists of a complex intertwining network of leaky capillaries due to the overexpression of different angiogenic factors but this is only a transient condition.The vessels rapidly acquire a pericyte layer and becomes open and clear from obstruction after several days. Angiogenesis at the sites of tissue repair appears to be rate limiting step as it is for a growing cancer. [33]

HALLMARK 5: RESISTING CELL DEATH

At any site of malignant cancer growth, there are various physiological stresses that, in healthy tissues, would trigger apoptosis. These include the signaling imbalances, hypoxic and reduced nutrient conditions which might be due to cancer therapeutics such as chemotherapy and radiotherapy. The apoptotic switches appear lowered in cancer cells [34].
Apoptosis is an important process involved in the early phases of wound healing (Greenhalgh, 1998; Wu and Chen, 2014). In normal wound healing, programmed cell death is necessary for removing inflammatory cells and formation of scar. This removal generally occurs without tissue damage or inflammation. [35]

HALLMARK 6: AVOIDING IMMUNE CELL DESTRUCTION

Cancer cells also avoid surveillance and destruction by both the innate and adaptive arms of the immune system. One of the key mechanisms whereby cancer cells evade immune cell destruction is by increasing the production of their inhibitory checkpoint molecules and this strategy has been recently highlighted as a therapeutic [reviewed in 36]
Some elements of an adaptive immune response are activated in a wound repair scenario. [37]However, the innate immune response is “clumsy” in comparison to the adaptive immune response and also nonspecific in its killing strategies.

HALLMARK 7: DEREGULATING CELLULAR ENERGETICS

Metabolism is a key player in repair, much as it is in cancer. In the 1960s [38] Inflammation is instrumental in both cancer and wound healing and it may be that inflammatory cell an important role as they might be key sensors of altered microenvironmental conditions, for example, hypoxia and mediators of changes to metabolic signalling in other cells [39]

CANCER HALLMARKS THAT MIGHT NOT BE SHARED BY REPAIRING TISSUES

All cancer hallmarksdo not have likely parallel in wound healing.However, it is believed that there are three hallmarks and enabling characteristics for cancer contrasting to wound healing.

1 AND 2. EVADING GROWTH SUPPRESSORS AND ENABLING REPLICATIVE IMMORTALITY

These two hallmarks of cancer are not clearly parallel to wound healing. The wound repair can be adjacent to 'evading growth suppressor' when some of the signalling pathways that enable proliferation and migration are temporarily epigenetically unsilenced but when the wound is repaired, they will epigenetically get silenced again whereas in developing cancer cells this process fails to occur. [40]
Likewise, there is no proof that wound repairing cells are deathless(immortal).The wound margin of fibroblast and epidermal cells might become older and recent studies have shown that the senescence-associated secretory phenotype (SASP) includes signals that are beneficial to repair. [41]

3. GENOMIC INSTABILITY AND MUTATION

Even, in this enabling characteristic of cancer it is not direct equivalent with tissue repair scenario unless one considers chronic wounds with their persistent inflammation, with probably excessive viral load and exposure to UV damage. This all can consequence to secondary mutations leading to neoplastic lesions in the vulnerable, exposed tissue [42].

SHARED HALLMARKS THAT ARE NOT AUTHENTIC CANCER HALLMARKS (YET)

The following mentioned hallmarks are considered as the enabling characteristics that promote both tumor development and wound healing.

1. THE MICROBIOME AND DYSBIOSIS

From birth, all external-facing human epithelial tissues, together with skin and gut, are occupied by bacteria that eventually establish homeostasis and symbiotic influence withlocal immune cells and systemic immunity [43].Disturbance of the microbiota is called as dysbiosis, which has been connected directly and indirectly in cancer development with the assumption that such changes will likely affect local inflammation to drive cancer initiation and progression[44].Alterations in the microbiome of tissues are generally considered to be potential activators rather than inhibitors of cancer progression, [45].A standard treatment for bladder cancer is to fill the bladder with Bacillus Calmette-Guerin, an attenuated strain of *Mycobacterium bovis* [46].Due to these infections somehow the host immune response is modulated to kill cancers.

It is believed that the wound microbiota might affect the efficiency of healing, for example the wild type mice and diabetic mice tend to have retarded healing but antimicrobial treatment can rapidly reverse this impairment [47].Commensal microbiota and the multiple cell types interaction is involved in cutaneous wound healing which regulates the immune response and promotes barrier restoration [48].

2. ABERRANT MATRIX DEPOSITION

Abnormal signalling in cancer cells can cause aberrant collagen deposition in tumors but this is also affected by inflammatory and other cells in the cancer microenvironment. Excessive matrix deposition is driven by TGF-β as well as by macrophages in aggressive breast cancer subtypes with increased collagen deposition[49].

In a wound scenario, it is clear that inflammation is vital and required for various aspects of adult healing, also causal for aberrant collagen deposition leading to a fibrotic wound scar.Fibrosis is driven by inflammation through various signalling pathways such as TGF-β1 and TGF-β2, both of which trigger the depositionof collagen and other matrix components by wound fibroblasts whereas blockingof TGF-β signalling at the wound site reduces the fibrotic response [50].

3. ADIPOCYTES: NOT SILENT BYSTANDERS

It is evident that obesity and cancer are linked together. During weight gain, adipocytes become hypertrophic and many die eventually. This triggers an accumulation of phagocytic macrophages that envelop dying adipocytes and form a crown-like structure (CLS) which are functionally and phenotypically different from adipocytes.[51](Figure3)

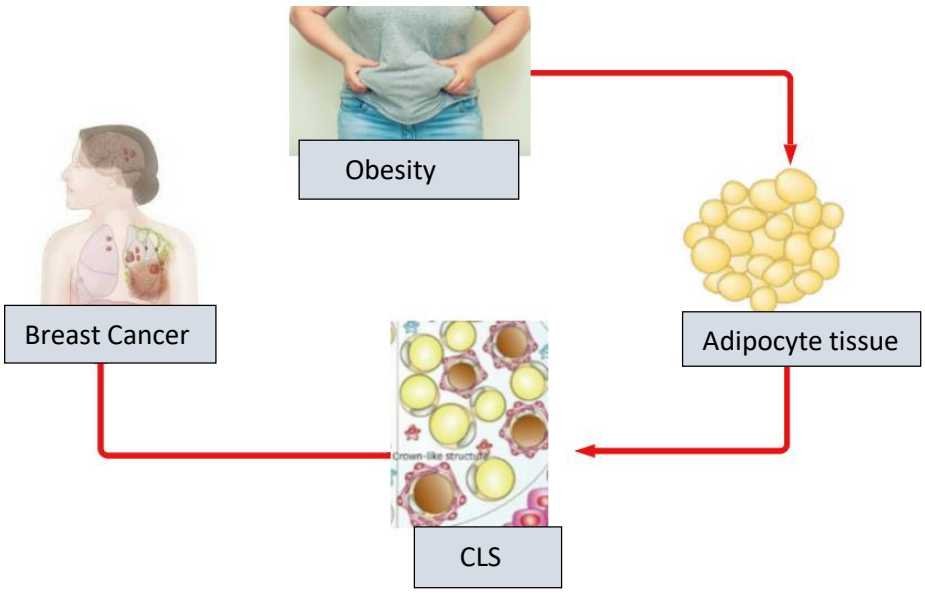
Positive CLS status is associated with a poor prognostic outcome in breast and prostate cancers and there is also evidence

for these structures having systemic endocrine effects on cancers at distant sites [52].

Obesity is also closely associated with type 2 diabetes and individual diabetic which are more prone to impaired wound healing (figure 4) as a consequence of poor vascularity, neuropathy and predisposition to infection because of chronic high blood glucose [53].

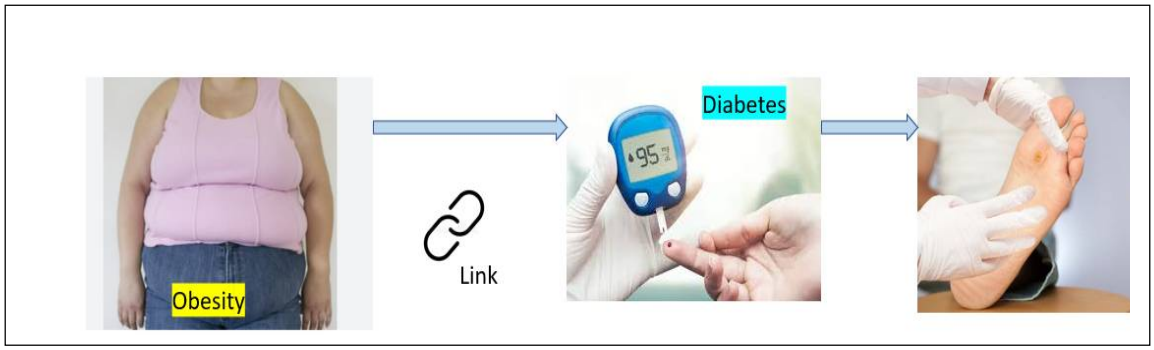
In a wound repair community, there is direct role of adipocytes and their preadipocyte precursors. [54].

Figure 3: Obesity affecting breast cancer



CLS – Crown like structure of adipocyte

Figure 4: Obesity associated with diabetic patient in wound repair



GROWTH FACTOR NETWORKS IN WOUND HEALING AND CANCER METASTASIS

The table explainseffect of common growth factors on various physiological processes in a healing wound and processes involved in cancer growth and metastasis.

Table 2:Role of common growth factors on regulation of various processes in a healing wound and cancer growth and metastasis. TGF-β decreases the proliferation of epithelial cells in both wound healing and cancer while promotes migration of keratinocytes in wound healing and tumour-promoting processes in cancer. [Reference 55]

GROWTH FACTOR	CELLULAR PROCESSES	
	CANCER	WOUND HEALING
Epidermal Growth Factor (EGF)	Cancer stem cells ↑ EMT ↑ Proliferation ↑ Stromal invasion ↑	Angiogenesis ↑ Migration ↑ Proliferation ↑
Transforming Growth Factor Beta (TGF-β)	Angiogenesis ↑ Chemoresistance ↑ Epithelial Mesenchymal Transition (EMT)↑ Stromal invasion ↑ **Proliferation ↓**	Migration ↑ **Proliferation ↓**
Fibroblast Growth Factor (FGF)	Angiogenesis ↑ Cancer stem cells ↑ Chemoresistance ↑ EMT ↑ Proliferation ↑	Angiogenesis ↑ Migration ↑ Proliferation ↑
Hepatocyte Growth Factor (HGF)	Angiogenesis ↑ Cancer stem cells ↑ Chemoresistance ↑ Proliferation ↑ Stromal invasion ↑	Angiogenesis ↑ Migration ↑ Proliferation ↑
Vascular Endothelial Growth Factor (VEGF)	Angiogenesis ↑ Cancer stem cells ↑ Proliferation ↑ Stromal invasion ↑	Angiogenesis ↑ Migration ↑ Proliferation ↑

CONCLUSION

Humanity's understanding of the interrelationship between epithelial wound healing and cancer has a long and extensive history, just as the two processes themselves have evolved and intertwined over phylogenetic time. [55]The flip side of drug repurposing has a reciprocal approach. It is to be considered that because of the multitude of shared mechanisms, any drug that might help to improveone aspect may also have unexpected consequences on the other.[56]

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CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

REFERENCES
1. .Nicole Antonio, Marie Louise Bønnelykke-Behrndtz, Laura Chloe Ward, John Collin, IbJarle Christensen, Torben Steiniche, Henrik Schmidt, Yi Feng, Paul Martin [2015]The wound inflammatory response exacerbates growth of pre-neoplastic cells and progression to cancer EMBO J;34(17):2219-36
2. H. F. Dvorak [1986]Tumors: wounds that do not heal. Similarities between tumor stroma generation and wound healing. The New England journal of medicine 315, 1650- 1659
3. H. F. Dvorak[2015] Tumors: wounds that do not heal-redux. Cancer immunology research 3, 1-11
4. F. Balkwill, A. Mantovani, [2001]Inflammation and cancer: back to Virchow? Lancet 357, 539-545
5. D. S. Foster, R. E. Jones, R. C. Ransom, M. T. Longaker, J. A. Norton[2018] The evolving relationship of wound healing and tumor stroma. JCI Insight 3,
6. M. Schäfer, S. Werner [2008]Cancer as an overhealing wound: an old hypothesis revisited. Nature Reviews Molecular Cell Biology 9, 628-638
7. M. A. Troester, M. H. Lee, M. Carter, C. Fan, D. W. Cowan, E. R. Perez, J. R. Pirone, C. M. Perou, D. J. Jerry, S. S. Schneider [2009] Activation of host wound responses in breast cancer microenvironment. Clin Cancer Res 15, 7020-7028
8. D. Hanahan, R. A. Weinberg [2011] Hallmarks of cancer: the next generation. Cell 144, 646- 674
9. D. Hanahan, R. A. Weinberg[2000] The hallmarks of cancer. Cell 100, 57-70
10. Morgane Macheret and Thanos D. Halazonetis[2015] DNA Replication Stress as a Hallmark of Cancer Annu. Rev. Pathol. Mech. Dis. 10:425–48
11. Tracey A. Martin, Lin Ye, Andrew J. Sanders, Jane Lane, and Wen G. Jiang [2013]Cancer Invasion and Metastasis: Molecular and Cellular Perspective Metastatic Cancer: Clinical and Biological Perspectives edited by Rahul Jandial.
12. Gemilang Khusnurrokhman, Farah Fatma Wati *[2022] Tumor-promoting inflammation in lung cancer: A literature review Annals of Medicine and Surgery 79: 104022
13. Jamal Majidpoor, Keywan Mortezaee[2019]Angiogenesis as a hallmark of solid tumors - clinical perspectives Cell Oncol (Dordr) 44(4):715-737
14. Courtney M. Townsend JR., MD, in Sabiston Textbook of Surgery, 2022 Tumor Biology and Tumor Markers Chapter 29, 656-686
15. Jonathan L. Messerschmidt, George C. Prendergast, Gerald L. Messerschmidt [2016] How Cancers Escape Immune Destruction and Mechanisms of Action for the New Significantly Active Immune Therapies: Helping Nonimmunologists Decipher Recent Advances, The Oncologist ;21:233–243
16. Tumor Cell Metabolism Pathways, Regulation and Biology, Sybille Mazurek · Maria Shoshan Editors Springer Wien Heidelberg New York Dordrecht London Chapter · December 2014 DOI: 10.1016/B978-0-12-386456-7.01912-2
17. Tony Gutschner and Sven Diederichs* [2012] The hallmarks of cancer A long non-coding RNA point of view RNA Biology Landes Bioscience; 9:6, 703-719
18. Yixin Yao, * and Wei Dai1 *[2014] Genomic Instability and Cancer J Carcinog Mutagen; 5: doi:10.4172/2157-2518.1000165
19. Joseph Vimal, Iris Himal& S. Kannan [2020] Role of microbial dysbiosis in carcinogenesis & cancer therapies Indian J Med Res 152, pp 553-561
20. Perlecan Zehra Elgundi *, Michael Papanicolaou, Gretel Major, Thomas R. Cox, James Melrose, John M. Whitelock and Brooke L. Farrugia *[2020] Cancer Metastasis: The Role of the Extracellular Matrix and the Heparan Sulfate Proteoglycan Frontiers in Oncology, Volume 9, Article 1482
21. Qi Wu, Bei Li, Zhiyu Li, Juanjuan Li, Si Sun* and Shengrong Sun* [2019] Cancer-associated adipocytes: key players in breast cancer progression, Journal of Hematology& Oncology pp 1-15
22. M. Najafi, A. Ahmadi, K. Mortezaee[2019] Extracellular-signal-regulated kinase/mitogenactivated protein kinase signaling as a target for cancer therapy: An updated review. Cell Biol. Int. 43, 1206–1222
23. J. A. Garlick, L. B. Taichman, [1994]Fate of human keratinocytes during reepithelialization in an organotypic culture model. Lab. Invest. 70, 916–924
24. G. Matoltsy, C. B. Viziam[1970] Further observations on epithelialization of small wounds: An autoradiographic study of incorporation and distribution of 3 H-thymidine in the epithelium covering skin wounds. J. Invest. Dermatol. 55, 20–25
25. G. Cory, Scratch-wound assay. Methods Mol. Biol. 769, 25–30 (2011).

26. N. Molinie, A. Gautreau [2018] Directional collective migration in wound healing assays. Methods Mol. Biol. 1749, 11–19
27. R. Grose, C. Hutter, W. Bloch, I. Thorey, F. M. Watt, R. Fassler, C. Brakebusch, S. Werner [2002] A crucial role of β1 integrins for keratinocyte migration in vitro and during cutaneous wound repair. Development 129, 2303–2315
28. Y. Feng, C. Santoriello, M. Mione, A. Hurlstone, P. Martin [2010] Live imaging of innate immune cell sensing of transformed cells in zebrafish larvae: Parallels between tumor initiation and wound inflammation. PLOS Biol. 8, e1000562
29. M. Lodyga, B. Hinz, [2020] TGF-β1 - A truly transforming growth factor in fibrosis and immunity. Semin. Cell Dev. Biol. 101, 123–139
30. C.-H. Heldin, J. Lennartsson, B. Westermark, [2018] Involvement of platelet-derived growth factor ligands and receptors in tumorigenesis. J. Intern. Med. 283, 16–44
31. J. Folkman [2006] Antiangiogenesis in cancer therapy--Endostatin and its mechanisms of action. Exp. Cell Res. 312, 594–607
32. R. R. Ramjiawan, A. W. Griffioen, D. G. Duda[2017]Anti-angiogenesis for cancer revisited: Is there a role for combinations with immunotherapy? Angiogenesis 20, 185–204
33. D. B. Gurevich, C. E. Severn, C. Twomey, A. Greenhough, J. Cash, A. M. Toye, H. Mellor, P. Martin [2018] Live imaging of wound angiogenesis reveals macrophage orchestrated vessel sprouting and regression. EMBO J. 37, e97786
34. J. M. Adams, S. Cory [2007] Bcl-2-regulated apoptosis: Mechanism and therapeutic potential. Curr. Opin. Immunol. 19, 488–496
35. Stefan Riwaldt, Thomas J. Corydon, Desiré Pantalone,Jayashree Sahana,Petra Wise, Markus Wehland,Marcus Krüger, Daniela Melnik, Sascha Kopp, Manfred Infanger, and Daniela Grimm [2021] Role of Apoptosis in Wound Healing and Apoptosis Alterations in Microgravity, Front Bioeng Biotechnol. ; 9: 679650.
36. M. C. Brunner-Weinzierl, C. E. Rudd [2018] CTLA-4 and PD-1 control of T-cell motility and migration: Implications for tumor immunotherapy. Front. Immunol. 9, 2737
37. W. L. Havran, J. M. Jameson [2010] Epidermal T cells and wound healing. J. Immunol. 184, 5423–5428
38. Q. P. Ghani, S. Wagner, M. Z. Hussain [2003] Role of ADP-ribosylation in wound repair. The contributions of Thomas K. Hunt, MD. Wound Repair Regen. 11, 439–444
39. S. A. Eming, T. A. Wynn, P. Martin [2017] Inflammation and metabolism in tissue repair and regeneration. Science 356, 1026–1030
40. T. Shaw, P. Martin, [2009]. Epigenetic reprogramming during wound healing: Loss of polycomb-mediated silencing may enable upregulation of repair genes, EMBO Rep. 10, 881–886.
41. P. Hiebert, M. S. Wietecha, M. Cangkrama, E. Haertel, E. Mavrogonatou, M.Stumpe, H. Steenbock, S. Grossi, H.-D. Beer, P. Angel, J. Brinckmann, D.Kletsas, J. Dengjel, S. Werner, [2018] Nrf2-mediated fibroblastre programming drives cellular senescence by targeting the matrisome. Dev.Cell 46, 145–161.e10.
42. F. M. Iqbal, Y. Sinha, W. Jaffe, [2015]Marjolin' s ulcer: A rare entity with a callfor early diagnosis:BMJ Case Rep. 2015, bcr2014208176.\
43. L. Byrd, Y. Belkaid, J. A. Segre, [2018] The human skin microbiome. Nat.Rev. Microbiol. 16,143–155.
44. Dzutsev, R. S. Goldszmid, S. Viaud, L. Zitvogel, G. Trinchieri, [2015] Therole of the microbiota in inflammation, carcinogenesis, and cancer therapy.Eur. J. Immunol. 45, 17–31.
45. S. Felgner, D. Kocijancic, M. Frahm, S. Weiss, [2016] Bacteria in cancer therapy: Renaissance of an old concept. Int J Microbiol, 8451728
46. Pettenati, M. A. Ingersoll, [2018] Mechanisms of BCG immunotherapy and its outlook for bladder cancer. Nat. Rev. Urol. 15, 615–625.
47. A. Holder, R. L. Brown, D. G. Greenhalgh, [1997]Mouse models to studywound closure and topical treatment of infected wounds in healing-impairedand normal healing hosts; Wound Repair Regen. 5, 198–204.
48. MarjanaTomic-Canic, Jamie L Burgess, Katelyn E ; Neill, NatasaStrbo, IrenaPastar[2020] Skin microbiota and its interplay with wound healing;
49. Acerbi, L. Cassereau, I. Dean, Q. Shi, A. Au, C. Park, Y. Y. Chen, J.Liphardt, E. S. Hwang, V. M. Weaver [2015]Human breast cancer invasionand aggression correlates with ECM stiffening and immune cell infiltration.IntegrBiol (Camb) 7, 1120–1134.
50. Kane, M. W. Ferguson, [1997] Transforming growth factors and wound healing. Int. J. Biochem. Cell Biol. 29, 63–78.
51. F. Quail, A. J. Dannenberg, [2019] The obese adipose tissue microenvironment in cancer development and progression. Nat. Rev.Endocrinol. 15, 139–154.
52. J. H. Stern, J. M. Rutkowski, P. E. Scherer [2016] Adiponectin, leptin andfatty acids in the maintenance of metabolic homeostasis through adiposetissue crosstalk. Cell Metab. 23, 770–784
53. P. Martin, R. Nunan [2015] Cellular and molecular mechanisms of repair inacute and chronic wound healing. Br. J. Dermatol. 173, 370–378

54. Franz, W. Wood, P. Martin [2018] Fat body cells are motile and actively migrate to wounds to drive repair and prevent infection. Dev. Cell 44, 460–470.
55. Gopinath M. Sundaram, Shan Quah and Prabha Sampath [2018] Cancer: the dark side of wound healing The FEBS Journal 285 4516–453 Federation of European Biochemical Societies
56. Lucy MacCarthy-Morrogh and Paul Martin [2020] Science Signaling | Review Wound Healing The hallmarks of cancer are also the hallmarks of wound healing Sci. Signal. 13, eaay8690

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