Supplementary Table 1a: Research studies for the role of mast cells in skin scarring in Animals			
Author	**Lesion type**	**Sample**	**Result**
Fetal skin scarring			
Wulff BC et al (2012)	Embryonic skin and wounds	FVB mice or C57BL/6J-KitW-v/J and WB/Rej KitW/J mice	Dermal mast cells in scarless wounds generated at embryonic day 15 (E15) are fewer in number, less mature, and do not degranulate in response to wounding as effectively as mast cells of fibrotic wounds made at embryonic day 18. Injection of mast cell lysates into E15 wounds disrupted scarless healing, suggesting that mast cells interfere with scarless repair. Scars were significantly smaller in mast cell-deficient Kit(W/W-v) mice compared with Kit(+/+) littermates. This data suggests that mast cells enhance scar formation, and that these cells may mediate the transition from scarless to fibrotic healing during fetal development.
Adult skin scarring			
Lateef Z et al (2019)	Thermal burns	C57Bl/6 mice	Toluidine blue staining indicated that mast cells disappeared following injury (likely due to degranulation) then increased in number thereafter in scars over 10 weeks post burns.
Zhu Z et al (2016)	Human skin transplants and injections of clodronate liposome	36 Male athymic nude mice	Significant reductions in mast cell infiltration were observed in the macrophage depletion with clodronate group compared to the control group.
Chen L et al (2014)	Normal skin and wounds	Female Balb/c mice	Compared to control, inhibition of mast cell activity, by disodium cromoglycate (DSCG), caused a significant decrease in scar width along with accelerated collagen re-organization. Tryptase β1 increased significantly in the course of wound healing. Blockade of mast cell activation reduces scar formation and inflammation without further weakening the healed wound.

Willenborg et al (2014)	Excisional skin injury	Genetic mouse model	The significant reduction of MC numbers does not affect skin wound healing and bleomycin-induced fibrosis in mice.
Nauta AC et al (2013)	Splinted excisional skin wounds	C57BL/6-Kit(W-sh/W-sh), WBB6F1-Kit(W/W-v), and Cpa3-Cre; Mcl-1(fl/fl) mice	Mast cell-deficient mice close excisional wounds at rates similar to those of the corresponding control mice and produce scars similar in size and collagen content compared to control mice. This data indicates that mast cells do not play a significant role in these features of the healing of splinted full thickness excisional cutaneous wounds in mice.
Yun IS et al (2012)	Full-thickness skin defects on the dorsal skin	Yorkshire pigs	Adipose-derived stem cells decrease the activity of mast cells.
Younan et al (2011)	Full-thickness wound surface microdeformations were induced by suction	Mast cell-deficient WWv mice	Wound tissue granulation, cell proliferation, blood vessel sprouting, and collagen maturation were found to be mast cell-dependent throughout the proliferating and remodeling stages of healing.
Shiota et al (2010)	Scald injury	Mast cell-deficient W/W(V) mice	The number of mast cells and chymase activity were very low in the injured tissues of W/W(V) mice. Wound healing after skin scald injury was partially impaired in mast cell-deficient mice. Mast cells may contribute to the wound healing process, especially in the proliferative and remodeling phases after scald injury.

Pathological skin scarring			
Ibrahim MM et al (2014)	Hypertrophic scar contracture	C57BL/6 mice	Mast cells were increased over 168 days compared to normal skin
Theoret CL et al (2013)	Equine exuberant granulation tissue and human keloids	Archival tissue samples of EGT (8) and keloid (12)	Macrophages and mast cells were infrequently found in both groups but polymorphonuclear cells were markedly increased in EGT.
Wang J et al (2011)	Skin grafting onto back of nude mice	Nude mice	Human skin grafted onto nude mice develops red raised and thickened scars having intrinsic properties that closely resemble hypertrophic scar formation as seen in humans. Split thickness skin grafting developed more scar than full thickness skin grafting. Grafting increased the infiltration of mast cells.
Aarabi et al (2007)	Hypertrophic scars in mice	Mice	Comparisons of murine scars with human scars demonstrated a duplication of all features of human hypertrophic scars including increased mast cell density.
Therapeutic approaches			
Horton et al (2013)	Radiation-induced fibrosis of skin/scars	C3H/HeN mice	Imatinib was shown to inhibit radiation-induced dermal fibrosis.
Orenstein et al (2010)	Synthetic mesh implantation	C57BL/6 J mice with and without cromolyn	Mast cell accumulation was seen at the periphery of inflammatory reactions, and in association with mesh-induced fibrosis and neovascularization. Cromolyn treatment resulted in significantly decreased fibrotic responses to all four meshes and reduced inflammation.
Zoog et al (2009)	imatinib mesylate applied to incisional wounds in mice	Mice	Imatinib which targets Ckit signalling has been shown to reduce mast cell recruitment in these skin wounds.

Gallant-Behm et al (2008)	Full-thickness excisional wounds	Yorkshire pigs	Mast cell stabilizer ketotifen may be an effective treatment for the reduction of excessive wound contraction and fibrosis.
Shiota et al (2005)	Fibrotic skin	Tight-skin (Tsk) mice.	A mast cell chymase inhibitor inhibited TGF-ß1 activation.

Supplementary Table 1b: Research studies for the role of mast cells in skin scarring in Humans			
Author	**Lesion type**	**Sample**	**Result**
Fetal skin scarring			
Walraven M et al (2016)	Second-trimester fetal skin versus adult skin	Ex vivo human skin samples	Second-trimester fetal skin contains low levels of immune cells including tryptase positive mast cells compared to adult skin
Gunin AG et al (2011)	Skin specimens from human fetuses and adult skin	Skin samples from foetuses and adult humans	The number of mast cells gradually increased with aging.
Adult skin scarring			
Trentin Brum S et al (2019)	Neurofibroma, mastocytosis, fibrous scar tissue	15 specimens of neurofibroma, 9 of mastocytosis, and 6 of fibrous scar tissue	Strong endoglin expression was found in the cytoplasmic granules of mast cells within the 3 groups. Similar results were observed with mast cell tryptase as well as toluidine blue. Endoglin may assist in the diagnosis and pathogenesis study of various processes associated with mast cells.
Glim JE et al (2015)	Human skin and oral mucosa, with or without scars	Ex vivo human skin and oral mucosa samples	No significant differences in mast cells were observed between skin and oral mucosa and both skin and oral mucosa scars contained equal numbers of mast cells when compared to healthy normal tissue.
White MJ et al (2015)	Human blood	In vitro	Tryptase and thrombin may be an initial trigger to override SAP inhibition of fibrocyte differentiation to initiate scar tissue formation.
Pistorio AL et al (2011)	Rodent derived peritoneal mast cell line (RMC-1) and	In vitro	Cx-43 participation was shown to be critical for gap junction intercellular communication between mast cells and fibroblasts, which may herald a novel direction for controlling fibrosis.

	human dermal derived fibroblasts		
Pathological skin scarring (Hypertrophic scars and keloid scars)			
Chen H et al (2017)	Hypertrophic scars	10 patients	Mast cell chymase promotes hypertrophic scar fibroblast proliferation and collagen synthesis by activating the TGF-β1/Smads signalling pathway
Arbi S et al (2015)	Keloid scars	Ex vivo human keloid samples	Keloid formation is primarily due to abnormal collagen synthesis where the consequent accumulation of collagen fibers causes increased mast cell recruitment and collagen phagocytosis. Subsequent release of mast cell-derived mediators then promotes further collagen synthesis.
Dong X et al (2014)	Normal skin and keloid fibroblasts	In vitro	Chymase promotes keloid fibroblast proliferation and collagen synthesis by activating TGF-β1. The activation of Smad protein signaling pathway by chymase is related to the elevated P-Smad protein expression in keloid fibroblasts.
Hellstrom M et al (2014)	Normal skin, keloids, hypertrophic scars and mature scars	20 patients	The frequency of mast cells found in keloids was lower than in other scar tissues and normal skin.
Gaber MA et al (2014)	Granulation tissues, surgical scars, hypertophic scars and keloid scars and healthy controls	50 patients	MCCs exhibited mild expression in normal tissue, granulation tissue, and surgical, hypertrophic and keloid scars. MCTs exhibited mild expression in normal tissue, granulation tissue and keloid, whereas moderate expression was exhibited in hypertrophic and surgical scars.

Choi et al (2013)	Hypertrophic scars and normal skin	38 patients	Increased number of mast cells present in hypertrophic scars compared to normal skin.
Foley TT et al (2013)	Human dermal fibroblasts	In vitro	Mast cells induce fibroblast activities associated with hypertrophic scarring through gap junctional intercellular communications. Eliminating the mast cell or its gap junctional intercellular communications with fibroblasts may be a possible approach in preventing hypertrophic scarring or reducing fibrotic conditions.
Ammendola M et al (2013)	Keloid scars and normotrophic scars	15 keloids and 10 normotrophic scars	Significant difference of microvascular density and number of mast cells positive to tryptase between keloids and normotrophic scars and a significant correlation in keloids. Tryptase-positive MCs might play a key role in keloids' angiogenesis.
Theoret CL et al (2013)	Equine exuberant granulation tissue and human keloids	Archival tissue samples of EGT (8) and keloid (12)	Macrophages and mast cells were infrequently found in both groups but polymorphonuclear cells were markedly increased in EGT.
Bagabir R et al (2012)	Keloid scars, normal scars and normal skin	25 keloids, 11 normal skin and 11 normal scar samples	Mature MCs (coexpressing OX40 ligand) were significantly increased in intralesional and perilesional KD sites compared with normal skin and scar tissue. This may implicate inflammation in the fibrotic process in KD.
Shaker SA et al (2011)	Keloid samples and normal skin controls	44 keloids	High number of mast cells observed in keloid tissues and were found in close contact with fibroblasts.
Har-Shai Y et al (2011)	Keloid scars biopsies before and after intralesional cryoneedle procedure	2 patients	The frozen tissue was devoid of proliferating cells and mast cells. The treatment reduced the number of proliferating cells, myofibroblasts and mast cells.

Therapeutic approaches			
Ud-Din S et al (2019)	Normal scars	62 healthy volunteers	Epigallocatechin-3-gallate topical formulation reduced mast cell numbers in normal skin scars between weeks 1-3 of application and this coincided with a reduction in scar thickness and an increase in scar elasticity with EGCG treatment
Sidgwick G et al (2016)	Normal scars and skin	Ex vivo skin samples	Histological analysis indicated a reduction in mast cell tryptase and chymase positive cell numbers in treated biopsies compared with untreated controls at day 7 and day 10.
Syed F et al (2013)	Keloid tissue and normal skin controls	Ex vivo human samples	EGCG induced epidermal shrinkage, reduced collagen-I and -III at mRNA and protein levels, depleted 98% of keloid-associated mast cells, and reduced the percentage of both cellularity and blood vessel count by week 4.
Mukhopadhyay A et al (2011)	Keloid and normal skin tissue	Ex vivo human samples and in vitro	SCF/c-KIT system played an important role in scar pathogenesis and Imatinib was identified as a key therapeutic agent for keloid scars.
Zhang et al (2006)	Keloid fibroblasts	In vitro	The interaction between mast cells and keloid fibroblasts contribute to excessive collagen accumulation in keloids and implied a therapeutic potential of green tea for the treatment of keloids.