8.

BÖLÜM

NONATEROSKLEROTİK TIKAYICI VASKÜLER HASTALIKLAR HAYVAN MODELLERİ

Ersin ÇELİK [1]

Aterosklerotik vasküler hastalıklar kadar sıklığı çok olmasa da non-aterosklerotik vasküler hastalıklar ile klinik pratikte hemen her gün karşılaşılmaktadır. Geniş bir klinik yelpazeye, çok çeşitli patolojik özelliklere sahip, organik ve vazospastik olan non-aterosklerotik vasküler hastalıkların bir kısmının etiyopatogenezi hala tam olarak anlaşılamamıştır (1). Tablo 1'de sınıflandırılması gösterilen non-aterosklerotik vasküler hastalıklar ile ilgili medikal, girişimsel ve cerrahi tedavi modalitelerini geliştirmek için daha çok klinik deneysel çalışma yapılması gerekmekte olup özellikle bazı alt gruplarda mevcut literatürde son derece az hayvan çalışması ve geliştirilmiş deneysel modellemeler mevcuttur.

Tablo 1: Non-aterosklerotik tıkayıcı vasküler hastalıkların sınıflandırılması

Non-Aterosklerotik Tıkayıcı Vasküler Hastalıklar	
Organik Hastalıklar	• Buerger Hastalığı • Takayasu Arteriti
Bağ Doku Hastalıkları (otoimmün arteritler)	• Behçet Hastalığı • Sistemik Lupus Eritematazus (SLE) • Skleroderma • Poliarteritis Nodosa
Vazospastik Hastalıklar	• Raynaud Sendromu • Akrosiyanozis • Livedo Retikularis • Frostbite (soğuk ısırması)
Hematolojik Hastalıklar	• Polisitemia Vera • Kriyoglobulinemi

[1] Uzm. Dr., Isparta Şehir Hastanesi, Kalp ve Damar Cerrahisi Kliniği

vaskülopati kliniği gelişir. Miks kriyoglobulinemilerde ise histopatolojik olarak immunkompleks birikimli vaskülit gelişir ve sistemik küçük damar vaskülitlerinin klinik bulguları ortaya çıkar (128).

Transgenik fareler ile yapılmış çeşitli çalışmalar literatürde bulunmakla birlikte, bu çalışmalarda kriyoglobulineminin böbrek, akciğer, dalak, karaciğer ve deri üzerine olan etkilerine bakılmıştır (129-132). Bu bağlamda kardiyak veya spesifik arteryel tutulum açısından geliştirilmiş yeterli deney hayvanı modellemeleri yoktur.

KAYNAKLAR

1. Haimovici, H., & Mishima, Y. (2012). Nonatherosclerotic diseases of small arteries. Haimovici's Vascular Surgery, 873-897.
2. Altuğ, T. (2009). Hayvan deneyleri etiği.
3. Olin, J. W. (2000). Thromboangiitis obliterans (Buerger's disease). New England Journal of Medicine, 343(12), 864-869.
4. Quintas, A., & Albuquerque, R. (2008). Buerger's disease: current concepts. Revista portuguesa de cirurgia cardio-toracica e vascular: orgao oficial da Sociedade Portuguesa de Cirurgia Cardio-Toracica e Vascular, 15(1), 33-40.
5. Matsushita, M., Shionoya, S., & Matsumoto, T. (1991). Urinary cotinine measurement in patients with Buerger's disease-effects of active and passive smoking on the disease process. Journal of vascular surgery, 14(1), 53-58.
6. Grassi, G., Seravalle, G., Calhoun, D. A., Bolla, G. B., Giannattasio, C., Marabini, M., ... & Mancia, G. (1994). Mechanisms responsible for sympathetic activation by cigarette smoking in humans. Circulation, 90(1), 248-253.
7. Buerger, L. (1908). Thrombo-Angiitis Obliterans: A Study of The Vascular Lesions Leading to Presenile Spontaneous Gangrene. 1. The American Journal of the Medical Sciences (1827-1924), 136(4), 567.
8. Kim, S. W., Han, H., Chae, G. T., Lee, S. H., Bo, S., Yoon, J. H., ... & Kang, K. S. (2006). Successful stem cell therapy using umbilical cord blood-derived multipotent stem cells for Buerger's disease and ischemic limb disease animal model. Stem cells, 24(6), 1620-1626.
9. Ashida, S. I., Ishihara, M., Ogawa, H., & Abiko, Y. (1980). Protective effect of ticlopidine on experimentally induced peripheral arterial occlusive disease in rats. Thrombosis research, 18(1-2), 55-67.
10. Wang, J., Wang, Y. S., & Fu, M. H. (1996). Experimental study on effects of mailuotong granule on anti-thromboangiitis obliterans. Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi= Chinese journal of integrated traditional and Western medicine, 16(7), 421-423.
11. Xu, Y., Zhang, R., Chen, J., Zhang, Q., Wang, J., Hu, J., ... & Guo, Y. (2009). Urocortin promotes the development of vasculitis in a rat model of thromboangiitis obliterans via corticotrophin-releasing factor type 1 receptors. British journal of pharmacology, 157(8), 1368-1379.
12. Hong, F., He, C., Liu, X., Tu, G., Guo, F., & Yang, S. (2011). Protective effect of Shenfu injection on thromboangiitis obliterans model rats. Journal of ethnopharmacology, 138(2), 458-462.
13. Liu, C., Kong, X., Wu, X., Wang, X., Guan, H., Wang, H., ... & Yuan, H. (2018). Alleviation of A disintegrin and metalloprotease 10 (ADAM10) on thromboangiitis obliterans involves the HMGB1/RAGE/NF-κB pathway. Biochemical and biophysical research communications, 505(1), 282-289.

14. Kong, X., Yuan, H., Wu, X., Zhang, J., Zhou, H., Wang, M., ... & Jin, X. (2013). High-mobility-group box protein 1 A box reduces development of sodium laurate-induced thromboangiitis obliterans in rats. Journal of vascular surgery, 57(1), 194-204.
15. Morgagni, J. B. (1761). De sedibus, et causis morborum per anatomen indagatis Libri quinque. Dissectiones, et animadversiones, nunc primum editas complectuntur propemodum innumeras (etc.) (Vol. 2). Remondini.
16. Ak, G., Seçkin, Ü., Borman, P., Özoran, K., & Coşkun, S. (2001). Takayasu Arteriti: 2 olgu nedeniyle. Fiziksel Tıp, 4, 43-6.
17. Arend, W. P., Michel, B. A., Bloch, D. A., Hunder, G. G., Calabrese, L. H., Edworthy, S. M., ... & Masi, A. T. (1990). The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis & Rheumatism, 33(8), 1129-1134.
18. Lupi-Herrera, E., Sanchez-Torres, G., Marcushamer, J., Mispireta, J., Horwitz, S., & Vela, J. E. (1977). Takayasu's arteritis. Clinical study of 107 cases. American heart journal, 93(1), 94-103.
19. Noris, M. (2001). Pathogenesis of Takayasu's arteritis. Journal of nephrology, 14(6), 506-513.
20. Conn, D. L. (1993). Vasculitis and related disorders. Textbook of rheumatology, 1079-1084.
21. Dhingra, R., Talwar, K. K., Chopra, P., & Kumar, R. (2005). An experimental design for induction of non-specific aortoarteritis. Indian Heart Journal, 57(2), 143-150.
22. Presti, R. M., Pollock, J. L., Dal Canto, A. J., O'Guin, A. K., & Virgin IV, H. W. (1998). Interferon γ regulates acute and latent murine cytomegalovirus infection and chronic disease of the great vessels. The Journal of experimental medicine, 188(3), 577-588.
23. Weck, K. E., Dal Canto, A. J., Gould, J. D., O'Guin, A. K., Roth, K. A., Saffitz, J. E., ... & Virgin, H. W. (1997). Murine γ-herpesvirus 68 causes severe large-vessel arteritis in mice lacking interferon-γ responsiveness: a new model for virus-induced vascular disease. Nature medicine, 3(12), 1346-1353.
24. Ueda, H., Saito, Y., Morooka, S., Ito, I., Yamaguchi, H., & Sugiura, M. (1968). Experimental arteritis produced immunologically in rabbits. Japanese heart journal, 9(6), 573-582.
25. Dal Canto, A. J., & Virgin Iv, H. W. (2000). Animal models of infection-mediated vasculitis: implications for human disease. International journal of cardiology, 75, S37-S45.
26. Fong, I. W., Chiu, B., Viira, E., Jang, D., Fong, M. W., Peeling, R., & Mahony, J. B. (1999). Can an Antibiotic (Macrolide) PreventChlamydia pneumoniae-Induced Atherosclerosis in a Rabbit Model?. Clin. Diagn. Lab. Immunol., 6(6), 891-894.
27. Zierhut, M., Mizuki, N., Ohno, S., Inoko, H., Gül, A., Onoe, K., & Isogai, E. (2003). Immunology and functional genomics of Behcet's disease. Cellular and Molecular Life Sciences CMLS, 60(9), 1903-1922.
28. Alpsoy, E., & Akman, A. (2007). Behçet Hastalığı: etyopatogenezde yeni kavramlar. Turkiye Klinikleri Journal of Internal Medical Sciences, 3(9), 8-14.
29. Ohno, S., Ohguchi, M., Hirose, S., Matsuda, H., Wakisaka, A., & Aizawa, M. (1982). Close association of HLA-Bw51 with Behcet's disease. Archives of ophthalmology, 100(9), 1455-1458.
30. Lehner, T. (1997). The role of heat shock protein, microbial and autoimmune agents in the aetiology of Behget's disease. International reviews of immunology, 14(1), 21-32.
31. Kaneko, F., Takahashi, Y., Muramatsu, Y., & Miura, Y. (1985). Immunological studies on aphthous ulcer and erythema nodosum-like eruptions in Behcet's disease. British Journal of Dermatology, 113(3), 303-312.
32. Karaki, S., Kariyone, A., Kato, N., Kano, K., Iwakura, Y., & Takiguchi, M. (1993). HLA-B51 transgenic mice as recipients for production of polymorphic HLA-A, B-specific antibodies. Immunogenetics, 37(2), 139-142.
33. Takeno, M., Kariyone, A. I., Yamashita, N., Takiguchi, M., Mizushima, Y., Kaneoka, H., & Sakane, T. (1995). Excessive function of peripheral blood neutrophils from patients with behcet's disease and from hla-b51 transgenic mice. Arthritis & Rheumatism, 38(3), 426-433.
34. Sohn, S. (1997). Etiopathology of Behçet's disease: herpes simplex virus infection and animal model. Yonsei medical journal, 38(6), 359-364.

35. Lee, S. I., Kwon, H. J., Lee, E. S., Yang, B. C., Bang, D., Lee, S., & Sohn, S. (2007). Using pCIN-mIL-4 DNA vector to express mRNA and protein and to improve herpes simplex virus-induced Behcet's disease symptoms in mice. Vaccine, 25(41), 7047-7055.
36. Lee, M., Choi, B., Kwon, H. J., Shim, J. A., Park, K. S., Lee, E. S., & Sohn, S. (2010). The role of Qa-2, the functional homolog of HLA-G, in a Behcet's disease-like mouse model induced by the herpes virus simplex. Journal of Inflammation, 7(1), 31.
37. Choi, B., Lee, E. S., & Sohn, S. (2011). Vitamin D3 ameliorates herpes simplex virus-induced Behcet's disease-like inflammation in a mouse model through down-regulation of Toll-like receptors. Clin exp rheumatol, 29(4 Suppl 67), S13-S19.
38. Zheng, Z., Sohn, S., Ahn, K. J., Bang, D., & Cho, S. B. (2015). Serum Reactivity Against Herpes Simplex Virus Type 1 UL48 Protein in Behçet's Disease Patients and a Behçet's Disease-like Mouse Model. Acta dermato-venereologica, 95(8), 952-958.
39. Islam, S. M., & Sohn, S. (2018). HSV-Induced Systemic Inflammation as an Animal Model for Behçet's Disease and Therapeutic Applications. Viruses, 10(9), 511.
40. Hammer, R. E., Maika, S. D., Richardson, J. A., Tang, J. P., & Taurog, J. D. (1990). Spontaneous inflammatory disease in transgenic rats expressing HLA-B27 and human β2m: an animal model of HLA-B27-associated human disorders. Cell, 63(5), 1099-1112.
41. Stanford, M. R., Kasp, E., Whiston, R., Hasan, A., Todryk, S., Shinnick, T., ... & Lehner, T. (1994). Heat shock protein peptides reactive in patients with Behçet's disease are uveitogenic in Lewis rats. Clinical & Experimental Immunology, 97(2), 226-231.
42. Ergüven, M., Tekin, E., Yılmaz, Ö., & Yıldız, N. (2007). Sistemik lupus eritematozus vakalarında klinik prezantasyon ve laboratuvar bulgularının değerlendirilmesi. Çocuk Dergisi, 7(4),240-246.
43. Theofilopoulos, A. N., & Dixon, F. J. (1985). Murine models of systemic lupus erythematosus. In Advances in immunology(Vol. 37, pp. 269-390). Academic Press.
44. Perry, D., Sang, A., Yin, Y., Zheng, Y. Y., & Morel, L. (2011). Murine models of systemic lupus erythematosus. BioMed Research International, 2011.
45. Theofilopoulos, A. N., & Dixon, F. J. (1985). Murine models of systemic lupus erythematosus. In Advances in immunology(Vol. 37, pp. 269-390). Academic Press.
46. Andrews, B. S., Eisenberg, R. A., Theofilopoulos, A. N., Izui, S., Wilson, C. B., McConahey, P. J., ... & Dixon, F. J. (1978). Spontaneous murine lupus-like syndromes. Clinical and immunopathological manifestations in several strains. The Journal of experimental medicine, 148(5), 1198-1215.
47. Maibaum, M. A., Haywood, M. E., Walport, M. J., & Morley, B. J. (2000). Lupus susceptibility loci map within regions of BXSB derived from the SB/Le parental strain. Immunogenetics, 51(4-5), 370-372.
48. Satoh, M., & Reeves, W. H. (1994). Induction of lupus-associated autoantibodies in BALB/c mice by intraperitoneal injection of pristane. The Journal of experimental medicine, 180(6), 2341-2346.
49. M. Satoh, A. Kumar, Y. S. Kanwar, and W. H. Reeves, "Anti-nuclear antibody production and immune-complex glomerulonephritis in BALB/c mice treated with pristane," Proceedings of the National Academy of Sciences of the United States of America, vol. 92, no. 24, pp. 10934–10938, 1995
50. Satoh, M., Richards, H. B., Shaheen, V. M., Yoshida, H., Shaw, M., Naim, J. O., ... & Reeves, W. H. (2000). Widespread susceptibility among inbred mouse strains to the induction of lupus autoantibodies by pristane. Clinical & Experimental Immunology, 121(2), 399-405.
51. Peixoto, T. V., Carrasco, S., Botte, D. A. C., Catanozi, S., Parra, E. R., Lima, T. M., ... & Goldenstein-Schainberg, C. (2019). CD4+ CD69+ T cells and CD4+ CD25+ FoxP3+ Treg cells imbalance in peripheral blood, spleen and peritoneal lavage from pristane-induced systemic lupus erythematosus (SLE) mice. Advances in Rheumatology, 59(1), 30.
52. Gunawan, M., Her, Z., Liu, M., Tan, S. Y., Chan, X. Y., Tan, W. W. S., ... & Chang, K. T. E. (2017). A novel human systemic lupus erythematosus model in humanised mice. Scientific reports, 7(1), 1-11.

53. Mollerberg, H. (1958). Attempts to produce the hydralazine syndrome in the albino rat. Acta medica Scandinavica, 161(6), 443-445.
54. Gardner, D. L. (1957). The response of the dog to oral L-hydrazinophthalazine (hydralazine). British journal of experimental pathology, 38(2), 227.
55. McCoy, F. W., & Leach, W. J. (1959). Experimental attempt to produce LE syndrome (arthritis) in swine with hydralazine. Proceedings of the Society for Experimental Biology and Medicine, 101(1), 183-183.
56. Braverman, I. M., & Lerner, A. B. (1962). Hydralazine disease in the guinea-pig as an experimental model for lupus erythematosus. Journal of Investigative Dermatology, 39(4), 317-327.
57. Choi, E., Shin, I., Youn, H., & Lee, C. (2004). Development of canine systemic lupus erythematosus model. Journal of Veterinary Medicine Series A, 51(7-8), 375-383.
58. Sharabi, A., Dayan, M., Zinger, H., & Mozes, E. (2010). A new model of induced experimental systemic lupus erythematosus (SLE) in pigs and its amelioration by treatment with a tolerogenic peptide. Journal of clinical immunology, 30(1), 34-44.
59. Chen, J., Zeng, W., Pan, W., Peng, C., Zhang, J., Su, J., ... & Wu, J. (2018). Symptoms of systemic lupus erythematosus are diagnosed in leptin transgenic pigs. PLoS biology, 16(8), e2005354.
60. LeRoy, E. C. (1988). Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. J rheumatol, 15, 202-205.
61. Nietert, P. J., & Silver, R. M. (2000). Systemic sclerosis: environmental and occupational risk factors. Current opinion in rheumatology, 12(6), 520-526.
62. Randone, S. B., Guiducci, S., & Cerinic, M. M. (2008). " Systemic sclerosis and infections." Autoimmun. Rev. 8 (1): 36-40.
63. LeRoy, E. C. (1996). Systemic sclerosis: a vascular perspective. Rheumatic Disease Clinics of North America, 22(4), 675-694.
64. Özdemir, F. (1999). Enflamatuvar Romatizmal Hastalıklarda Semptomlar, Bulgular ve Sistemik Sorunlar. Türk Fiz Tıp Rehab Derg, 2(Suppl 1), 6-23.
65. Matei, A. E., Chen, C. W., Kiesewetter, L., Györfi, A. H., Li, Y. N., Trinh-Minh, T., ... & Jüngel, A. (2019). Vascularised human skin equivalents as a novel in vitro model of skin fibrosis and platform for testing of antifibrotic drugs. Annals of the rheumatic diseases, 78(12), 1686-1692.
66. Gershwin, M. E., Abplanalp, H., Castles, J. J., Ikeda, R. M., Van der Water, J., Eklund, J., & Haynes, D. (1981). Characterization of a spontaneous disease of white leghorn chickens resembling progressive systemic sclerosis (scleroderma). The Journal of experimental medicine, 153(6), 1640-1659.
67. Van De Water, J., Boyd, R., Wick, G., & Gershwin, M. E. (1994). The immunologic and genetic basis of avian scleroderma, an inherited fibrotic disease of line 200 chickens. International reviews of immunology, 11(3), 273-282.
68. Gruschwitz, M. S., Moormann, S., Krömer, G., Sgonc, R., Dietrich, H., Boeck, G., ... & Wick, G. (1991). Phenotypic analysis of skin infiltrates in comparison with peripheral blood lymphocytes, spleen cells and thymocytes in early avian scleroderma. Journal of autoimmunity, 4(4), 577-593.
69. Ausserlechner, M. J., Sgonc, R., Dietrich, H., & Wick, G. (1997). Altered procollagen mRNA expression during the progression of avian scleroderma. Molecular Medicine, 3(10), 654-662.
70. Cipriani, P., Di Benedetto, P., Dietrich, H., Ruscitti, P., Liakouli, V., Carubbi, F., ... & Giacomelli, R. (2016). Searching for a good model for systemic sclerosis: the molecular profile and vascular changes occurring in UCD-200 chickens strongly resemble the early phase of human systemic sclerosis. Archives of medical science: AMS, 12(4), 828.
71. Birgani, S. A., Mailänder, M., Wasle, I., Dietrich, H., Gruber, J., Distler, O., & Sgonc, R. (2016). Efficient therapy of ischaemic lesions with VEGF121-fibrin in an animal model of systemic sclerosis. Annals of the rheumatic diseases, 75(7), 1399-1406.

72. Kerje, S., Hellman, U., Do, L., Larsson, G., Kämpe, O., Engström-Laurent, A., & Lindqvist, U. (2016). Is low molecular weight hyaluronan an early indicator of disease in avian systemic sclerosis?. Connective tissue research, 57(5), 337-346.
73. Siracusa, L. D., McGrath, R., Ma, Q., Moskow, J. J., Manne, J., Christner, P. J., ... & Jimenez, S. A. (1996). A tandem duplication within the fibrillin 1 gene is associated with the mouse tight skin mutation. Genome Research, 6(4), 300-313.
74. Green, M. C., Sweet, H. O., & Bunker, L. E. (1976). Tight-skin, a new mutation of the mouse causing excessive growth of connective tissue and skeleton. The American journal of pathology, 82(3), 493.
75. Menton, D. N., & Hess, R. A. (1980). The ultrastructure of collagen in the dermis of tight-skin (Tsk) mutant mice. Journal of Investigative Dermatology, 74(3), 139-147.
76. Menton, D. N., Hess, R. A., Lichtenstein, J. R., & Eisen, A. Z. (1978). The Structure And Tensile Properties of The Skin Tight-Skin(Tsk) Mutant Mice. Journal of Investigative Dermatology, 70(1), 4-10.
77. Christner, P. J., Peters, J., Hawkins, D., Siracusa, L. D., & Jimenez, S. A. (1995). The tight skin 2 mouse. Arthritis & Rheumatism, 38(12), 1791-1798.
78. Gentiletti, J., McCloskey, L. J., Artlett, C. M., Peters, J., Jimenez, S. A., & Christner, P. J. (2005). Demonstration of autoimmunity in the tight skin-2 mouse: a model for scleroderma. The Journal of Immunology, 175(4), 2418-2426.
79. Muggia, F. M., Louie, A. C., & Sikic, B. I. (1983). Pulmonary toxicity of antitumor agents. Cancer treatment reviews, 10(4), 221-243.
80. Finch, W. R., Rodnan, G. P., Buckingham, R. B., Prince, R. K., & Winkelstein, A. (1980). Bleomycin-induced scleroderma. The Journal of rheumatology, 7(5), 651-659.
81. Yamamoto, T. (2017). Animal Models of Systemic Sclerosis. In Animal Models for the Study of Human Disease(pp. 951-966). Academic Press.
82. Yoshizaki, A., Yanaba, K., Yoshizaki, A., Iwata, Y., Komura, K., Ogawa, F., ... & Fujimoto, M. (2010). Treatment with rapamycin prevents fibrosis in tight-skin and bleomycin-induced mouse models of systemic sclerosis. Arthritis & Rheumatism, 62(8), 2476-2487.
83. Ishikawa, H., Takeda, K., Okamoto, A., Matsuo, S. I., & Isobe, K. I. (2009). Induction of autoimmunity in a bleomycin-induced murine model of experimental systemic sclerosis: an important role for CD4+ T cells. Journal of investigative dermatology, 129(7), 1688-1695.
84. McCullough, B. (1978). Bleomycin-induced diffuse interstitial pulmonary fibrosis in baboons. The Journal of clinical investigation, 61(1), 79-88.
85. Collins, J. F., Mccullough, B., Coalson, J. J., & Johanson Jr, W. G. (1981). Bleomycin-induced diffuse interstitial pulmonary fibrosis in baboons. II. Further studies on connective tissue changes. American Review of Respiratory Disease, 123(3), 305-312.
86. Goldstein, R. H., Lucey, E. C., Franzblau, C., & Snider, G. L. (1979). Failure of mechanical properties to parallel changes in lung connective tissue composition in bleomycin-induced pulmonary fibrosis in hamsters. American Review of Respiratory Disease, 120(1), 67-73.
87. Callado, M. R., Viana, V. S., Vendramini, M. B., Leon, E. P., Bueno, C., Velosa, A. P., ... & Yoshinari, N. H. (2007). Autoantibody profile in the experimental model of scleroderma induced by type V human collagen. Immunology, 122(1), 38-46.
88. Velosa, A. P. P., Teodoro, W. R., dos Anjos, D. M., Konno, R., Oliveira, C. C., Katayama, M. L., ... & Yoshinari, N. H. (2010). Collagen V-induced nasal tolerance downregulates pulmonary collagen mRNA gene and TGF-beta expression in experimental systemic sclerosis. Respiratory research, 11(1), 1.
89. Eferl, R., Hasselblatt, P., Rath, M., Popper, H., Zenz, R., Komnenovic, V., ... & Wagner, E. F. (2008). Development of pulmonary fibrosis through a pathway involving the transcription factor Fra-2/AP-1. Proceedings of the National Academy of Sciences, 105(30), 10525-10530.
90. Reich, N., Maurer, B., Akhmetshina, A., Venalis, P., Dees, C., Zerr, P., ... & Distler, O. (2010). The transcription factor Fra-2 regulates the production of extracellular matrix in systemic

sclerosis. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 62(1), 280-290.

91. Sonnylal, S., Denton, C. P., Zheng, B., Keene, D. R., He, R., Adams, H. P., ... & De Crombrugghe, B. (2007). Postnatal induction of transforming growth factor β signaling in fibroblasts of mice recapitulates clinical, histologic, and biochemical features of scleroderma. Arthritis & Rheumatism, 56(1), 334-344.
92. Denton, C. P., Zheng, B., Evans, L. A., Shi-wen, X., Ong, V. H., Fisher, I., ... & de Crombrugghe, B. (2003). Fibroblast-specific expression of a kinase-deficient type II transforming growth factor β (TGFβ) receptor leads to paradoxical activation of TGFβ signaling pathways with fibrosis in transgenic mice. Journal of Biological Chemistry, 278(27), 25109-25119.
93. Derrett-Smith, E. C., Dooley, A., Khan, K., Shi-Wen, X., Abraham, D., & Denton, C. P. (2009). Aortic Smooth Muscle Cells Show a Pro-Fibrotic Phenotype in a TGF-Beta Dependant Mouse Model of Systemic Sclerosis. Arthritis and Rheumatism, 60(S10), 1061-1061.
94. Kasper, M., Reimann, T., Hempel, U., Wenzel, K. W., Bierhaus, A., Schuh, D., ... & MŘller, M. (1997). Loss of caveolin expression in type I pneumocytes as an indicator of subcellular alterations during lung fibrogenesis. Histochemistry and cell biology, 109(1), 41-48.
95. Drab, M., Verkade, P., Elger, M., Kasper, M., Lohn, M., Lauterbach, B., ... & Schedl, A. (2001). Loss of caveolae, vascular dysfunction, and pulmonary defects in caveolin-1 gene-disrupted mice. Science, 293(5539), 2449-2452.
96. Razani, B., Engelman, J. A., Wang, X. B., Schubert, W., Zhang, X. L., Marks, C. B., ... & Di Vizio, D. (2001). Caveolin-1 null mice are viable but show evidence of hyperproliferative and vascular abnormalities. Journal of Biological Chemistry, 276(41), 38121-38138.
97. Park, D. S., Cohen, A. W., Frank, P. G., Razani, B., Lee, H., Williams, T. M., ... & Jelicks, L. A. (2003). Caveolin-1 null (−/−) mice show dramatic reductions in life span. Biochemistry, 42(51), 15124-15131.
98. Murata, T., Lin, M. I., Huang, Y., Yu, J., Bauer, P. M., Giordano, F. J., & Sessa, W. C. (2007). Reexpression of caveolin-1 in endothelium rescues the vascular, cardiac, and pulmonary defects in global caveolin-1 knockout mice. The Journal of experimental medicine, 204(10), 2373-2382.
99. Colmegna, I., & Maldonado-Cocco, J. A. (2005). Polyarteritis nodosa revisited. Current rheumatology reports, 7(4), 288-296.
100. Ozen, S., Besbas, N., Saatci, U., & Bakkaloglu, A. (1992). Diagnostic criteria for polyarteritis nodosa in childhood. The Journal of pediatrics, 120(2), 206-209.
101. Pagnoux, C., Cohen, P., & Guillevin, L. (2006). Vasculitides secondary to infections. Clinical and experimental rheumatology, 24(2), S71.
102. Samarkos, M., Loizou, S., Vaiopoulos, G., & Davies, K. A. (2005, October). The clinical spectrum of primary renal vasculitis. In Seminars in arthritis and rheumatism(Vol. 35, No. 2, pp. 95-111). WB Saunders.
103. Bakkaloglu, A., Ozen, S., Baskin, E., Besbas, N., Gur-Guven, A., Kasapcopur, O., & Tinaztepe, K. (2001). The significance of antineutrophil cytoplasmic antibody in microscopic polyangitis and classic polyarteritis nodosa. Archives of disease in childhood, 85(5), 427-430.
104. Wigley, R. D., & Couchman, K. G. (1966). Polyarteritis nodosa-like disease in outbred mice. Nature, 211(5046), 319-320.
105. Arison, R. N., & Feudale, E. L. (1967). Induction of renal tumour by streptozotocin in rats. Nature, 214(5094), 1254-1255.
106. Baczako, K., & Dolderer, M. (1997). Polyarteritis nodosa-like inflammatory vascular changes in the pancreas and mesentery of rats treated with streptozotocin and nicotinamide. Journal of comparative pathology, 116(2), 171-180.
107. Suzuki, T., Motoyama, T. I., & Sato, R. (1980). Periarteritis Nodosa In Spontaneously Hypertensive Rats:–Immunohistological Study and Permeability Test–. Pathology International, 30(6), 907-915.
108. Haimovici, H., & Mishima, Y. (2012). Nonatherosclerotic diseases of small arteries. Haimovici's Vascular Surgery, 873-897.

109. Kadan, M., Karabacak, K., & Erkan, Kaya. Vazospastik Damar Hastalıkları. Turkish Journal of Vascular Surgery, 22(2).
110. Sarı, E. Frostbite Injury During Tattoo Treatment: Case Report and Summary of the Literature.
111. Koljonen, V., Andersson, K., Mikkonen, K., & Vuola, J. (2004). Frostbite injuries treated in the Helsinki area from 1995 to 2002. Journal of Trauma and Acute Care Surgery, 57(6), 1315-1320.
112. Auerbach, L. J., Galvez, M. G., De Clerck, B. K., Glotzbach, J., Wehner, M. R., Chang, E. I., ... & Auerbach, P. S. (2013). A novel mouse model for frostbite injury. Wilderness & environmental medicine, 24(2), 94-104.
113. Goertz, O., Hirsch, T., Buschhaus, B., Daigeler, „ Vogelpohl, J., Langer, S., ... & Ring, A. (2011). Intravital pathophysiologic comparison of frostbite and burn injury in a murine model. Journal of Surgical Research, 167(2), e395-e401.
114. Corn, C. C., Malone, J. M., Wachtel, T. L., Robson, M. C., Hayward, P. G., Chou, L. S., & Francis, K. (1991). The protection against and treatment of a liquid propane freeze injury: an experimental model. The Journal of burn care & rehabilitation, 12(6), 516-520.
115. Aizawa, T., Kuwabara, M., Kubo, S., Aoki, S., Azuma, R., & Kiyosawa, T. (2019). Protective Effect of Extract of Ginkgo biloba 761 against Frostbite Injury in Rats. Plastic and reconstructive surgery, 143(6), 1657-1664.
116. Hardenbergh, E., & Miles, J. A. (1972). The effect of sympathectomy on tissue loss after experimental frostbite of the rabbit ear. Journal of Surgical Research, 13(3), 126-134.
117. Salimi, Z., Wolverson, M. K., Herbold, D. R., & Vas, W. (1986). Frostbite: experimental assessment of tissue damage using Tc-99m pyrophosphate. Work in progress. Radiology, 161(1), 227-231.
118. Sarikaya, I., Aygit, A. C., Candan, L., Sarikaya, A., Türkyilmaz, M., & Berkarda, Ş. (2000). Assessment of tissue viability after frostbite injury by technetium-99m-sestamibi scintigraphy in an experimental rabbit model. European journal of nuclear medicine, 27(1), 41-45.
119. Uygur, F., Noyan, N., Sever, C., & Gümüş, T. (2009). The current analysis of the effect of hyperbaric oxygen therapy on the frostbitten tissue: Experimental study in rabbits. Open Medicine, 4(2), 198-202.
120. Schoning, P., Hall, S. M., & Hamlet, M. P. (1990). Experimental frostbite: freezing times, rewarming times, and lowest temperatures of pig skin exposed to chilled air. Cryobiology, 27(2), 189-193.
121. Rothenberger, J., Held, M., Jaminet, P., Schiefer, J., Petersen, W., Schaller, H. E., & Rahmanian-Schwarz, A. (2014). Development of an animal frostbite injury model using the Goettingen-Minipig. Burns, 40(2), 268-273.
122. Pearson, T. C., Messinezy, M., Westwood, N., Green, A. R., Bench, A. J., Green, A. R., ... & Finazzi, G. (2000). A polycythemia vera update: diagnosis, pathobiology, and treatment. ASH Education Program Book, 2000(1), 51-68.
123. Bolaman, Z. (2009). Turkiye Klinikleri Hematology-Special Topics, 2(3), 9-26.
124. Zaleskas, V. M., Krause, D. S., Lazarides, K., Patel, N., Hu, Y., Li, S., & Van Etten, R. A. (2006). Molecular pathogenesis and therapy of polycythemia induced in mice by JAK2 V617F. PloS one, 1(1).
125. Kubovcakova, L., Lundberg, P., Grisouard, J., Hao-Shen, H., Romanet, V., Andraos, R., ... & Skoda, R. C. (2013). Differential effects of hydroxyurea and INC424 on mutant allele burden and myeloproliferative phenotype in a JAK2-V617F polycythemia vera mouse model. Blood, The Journal of the American Society of Hematology, 121(7), 1188-1199.
126. Jin, X., Zhao, W., Kirabo, A., Park, S. O., Ho, W. T., Sayeski, P. P., & Zhao, Z. J. (2014). Elevated levels of mast cells are involved in pruritus associated with polycythemia vera in JAK2V617F transgenic mice. The Journal of Immunology, 193(2), 477-484.

127. Ma, A. C., Fan, A., Ward, A. C., Liongue, C., Lewis, R. S., Cheng, S. H., ... & Leung, A. Y. (2009). A novel zebrafish jak2aV581F model shared features of human JAK2V617F polycythemia vera. Experimental hematology, 37(12), 1379-1386.
128. Yazisiz, V. (2018). Kriyoglobulinemi. Turkiye Klinikleri Hematology-Special Topics, 11(2), 185- 192.
129. Taneda, S., Segerer, S., Hudkins, K. L., Cui, Y., Wen, M., Segerer, M., ... & Alpers, C. E. (2001). Cryoglobulinemic glomerulonephritis in thymic stromal lymphopoietin transgenic mice. The American journal of pathology, 159(6), 2355-2369.
130. Taneda, S., Hudkins, K. L., Cui, Y., Farr, A. G., Alpers, C. E., & Segerer, S. (2003). Growth factor expression in a murine model of cryoglobulinemia. Kidney international, 63(2), 576-590.
131. Trendelenburg, M., Fossati-Jimack, L., Cortes-Hernandez, J., Turnberg, D., Lewis, M., Izui, S., ... & Botto, M. (2005). The role of complement in cryoglobulin-induced immune complex glomerulonephritis. The Journal of Immunology, 175(10), 6909-6914.
132. Gyotoku, Y., Abdelmoula, M., Spertini, F., Izui, S., & Lambert, P. H. (1987). Cryoglobulinemia induced by monoclonal immunoglobulin G rheumatoid factors derived from autoimmune MRL/MpJ-lpr/lpr mice. The Journal of Immunology, 138(11), 3785-3792.