Spontaneous and induced dermal lesions in rodents, rabbits and minipigs.

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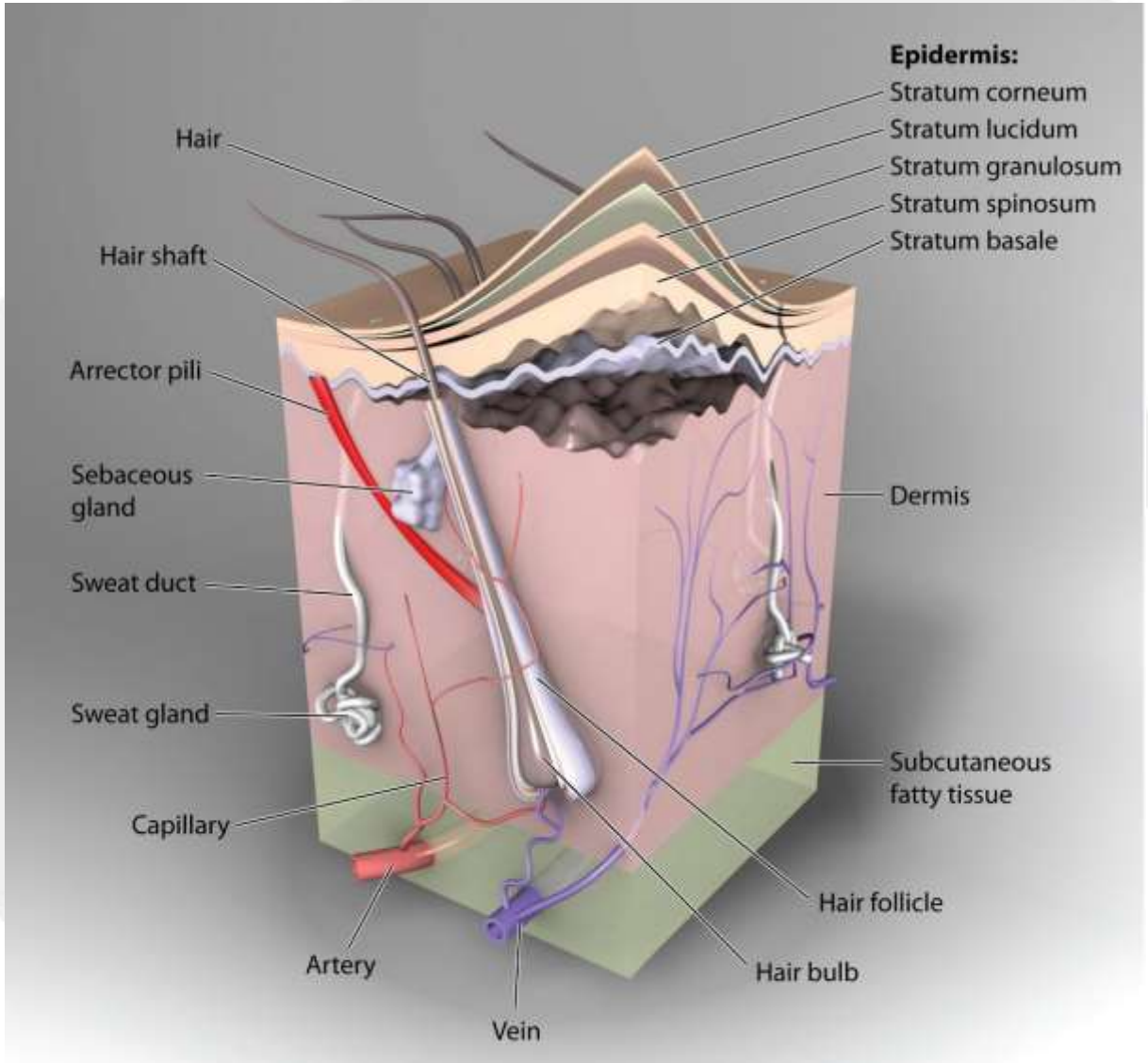
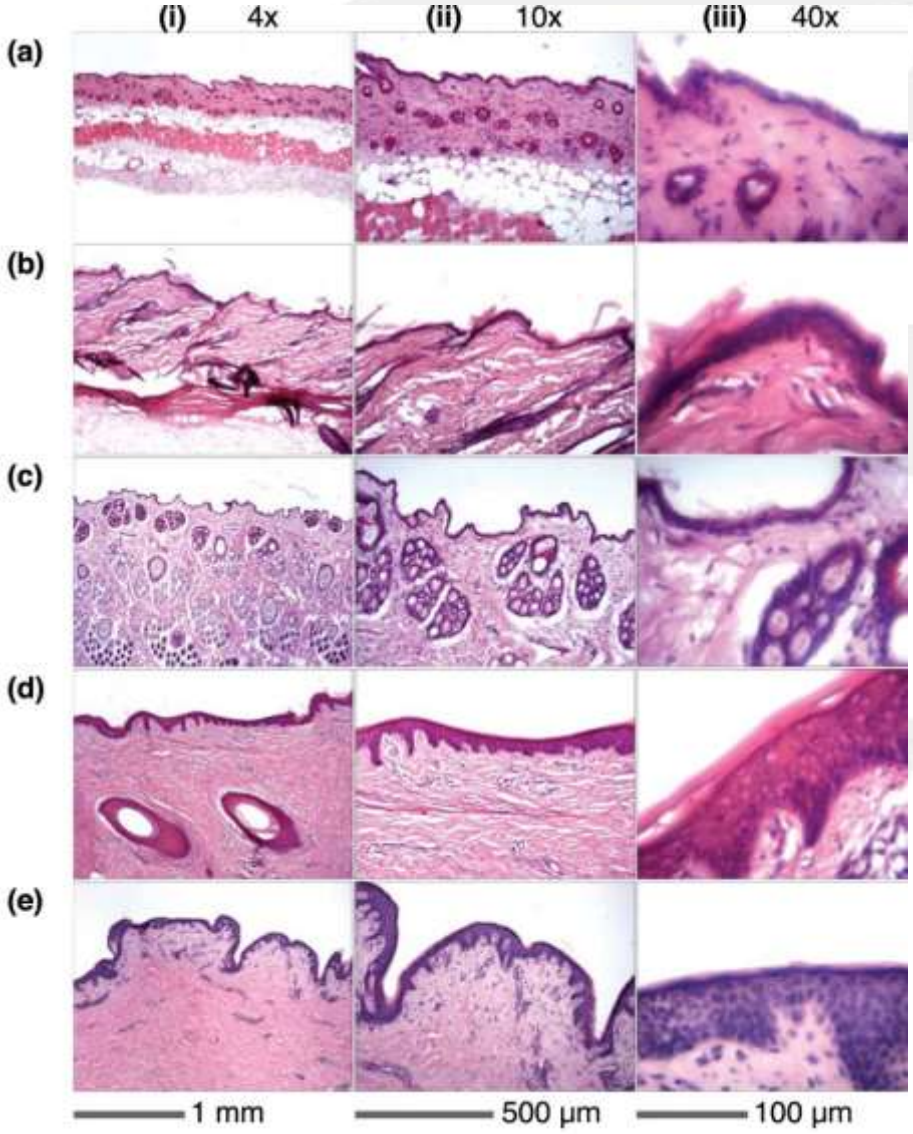
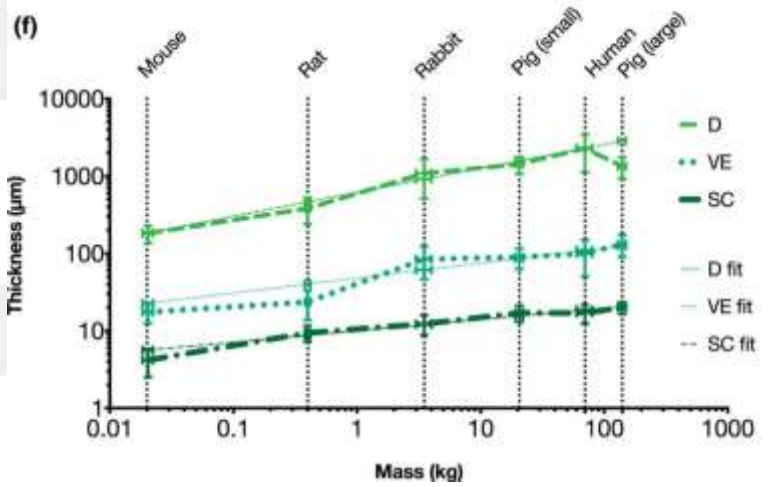
General morphological aspects



http://stevegallik.org/sites/histologyolm.stevegallik.org/images/skinlayers.jpg

Species differences: morphology/sensory



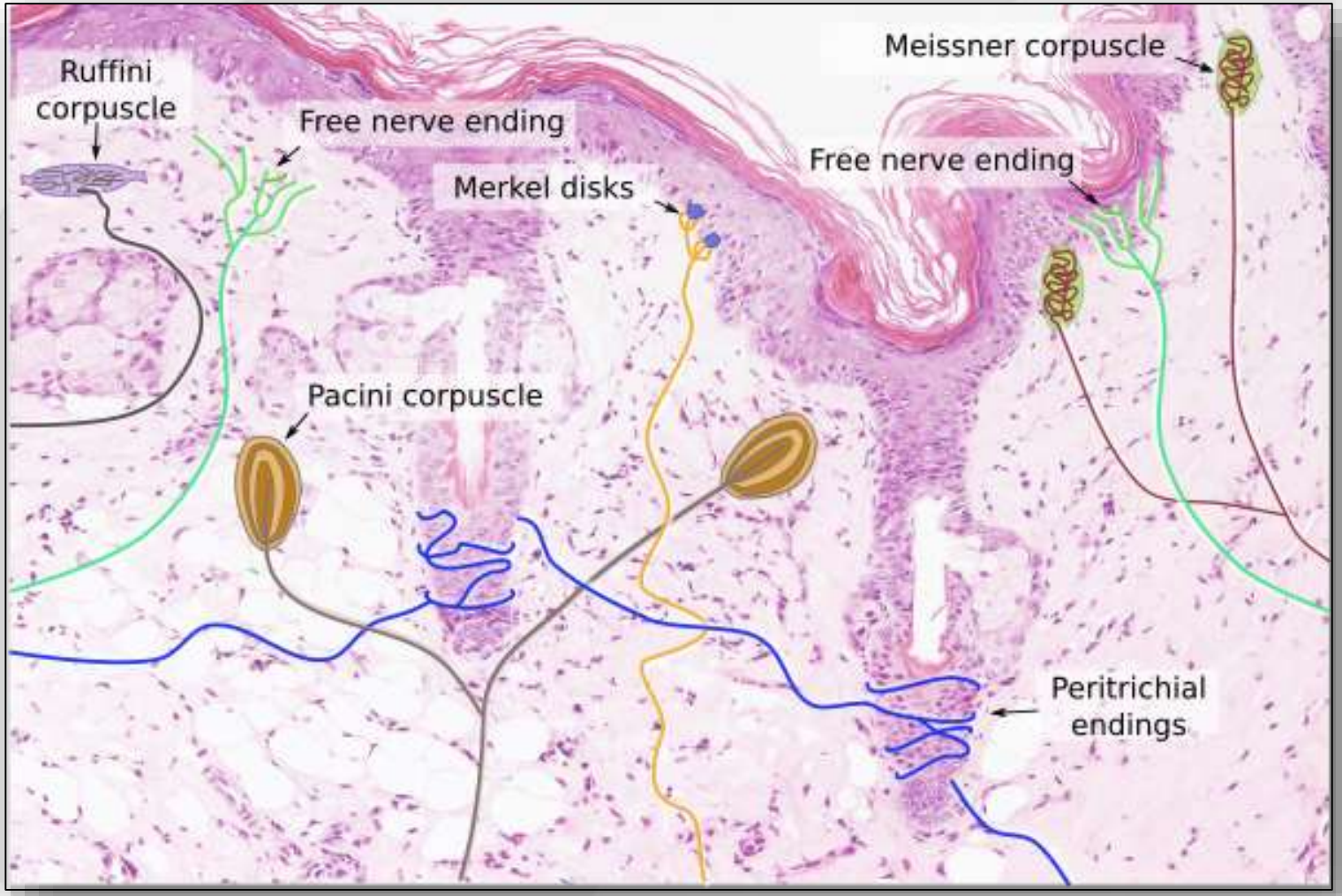


Wei JCJ et a., 2017.
Allometric scaling of skin thickness, elasticity, viscoelasticity to mass for micro-medical device translation: from mice, rats, rabbits, pigs to humans. Sci Rep. 2017 Nov 21;7(1):15885

General morphological aspects

https://i.ytimg.com/vi/acXjaANVK4M/maxresdefault.jpg

Sensitivity



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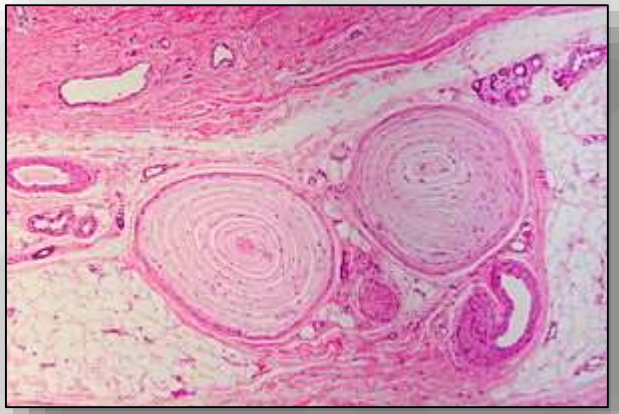
Species differences: morphology/sensory



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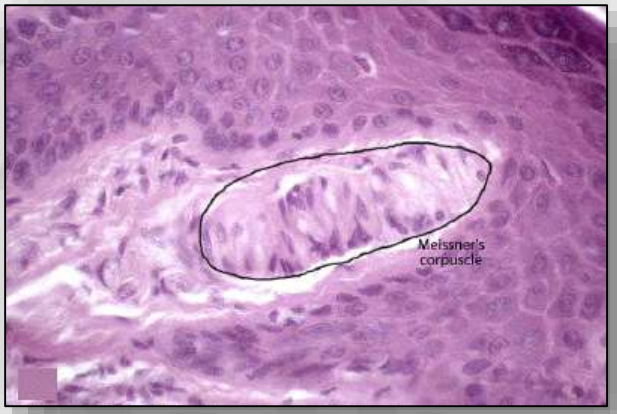

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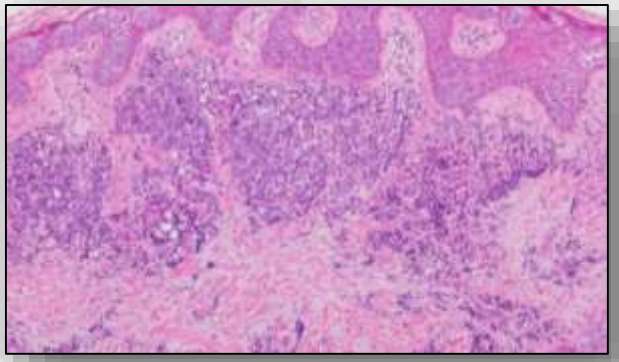
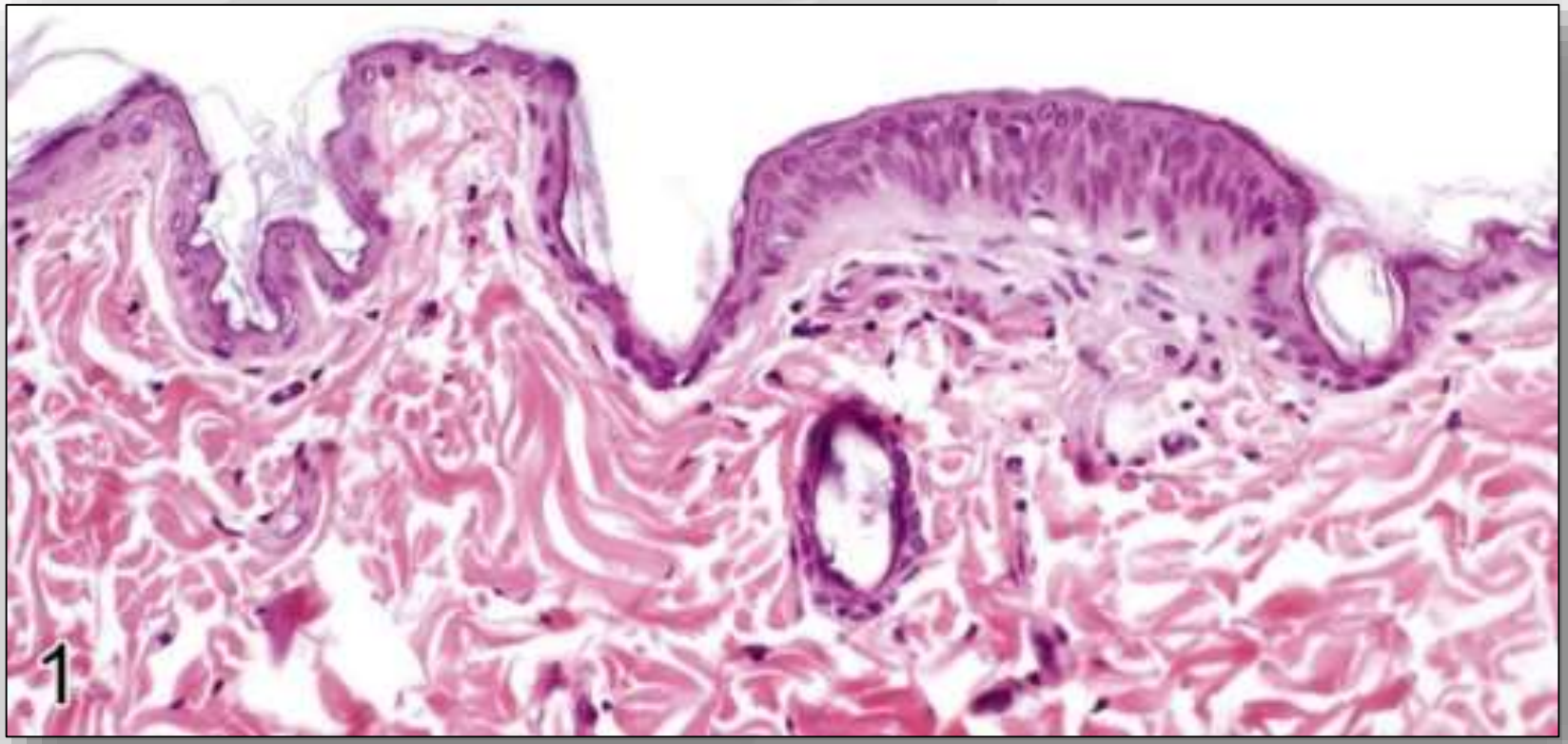


http://www.pathologyoutlines.com/caseofweek/case304image2.jpg

https://thumbor.kenhub.com/ARWp216PnxNUK6GmaKMzEzark_8=/fit-in/800x1600/filters:watermark

Species differences: morphology/sensory



https://openi.nlm.nih.gov/imgs/512/123/4091526/PMC4091526_tox-26-S027-g001.png

Non-Neoplastic Lesions: Rats

Non-Neoplastic lesions: Example, Rat. Males 28-D

Male	Total n	Mean %	SD %	Female	Total n	Mean %	SD %
Numbers of rats examined	834			Numbers of rats examined	899		
Congestion	1	0.91	9.53	Congestion	0	0.00	0.00
Hemorrhage	1	0.05	0.48	Hemorrhage	0	0.00	0.00
Mononuclear cell foci	7	0.73	3.51	Mononuclear cell foci	4	0.37	1.91
Inflammatory cell infiltration	5	1.21	7.77	Inflammatory cell infiltration	5	0.59	4.71
Scab formation	3	0.73	5.20	Scab formation	1	0.19	1.93
Necrosis	1	0.91	9.53	Necrosis	0	0.00	0.00
Abscess	1	0.09	0.95	Abscess	0	0.00	0.00
Ulceration	2	0.64	5.12	Ulceration	1	0.09	0.97
Folliculitis	1	0.18	1.91	Folliculitis	1	0.00	0.00
Inflammation	5	2.09	13.48	Inflammation	4	0.37	3.05
Fibrosis	1	0.18	1.91	Fibrosis	2	0.19	1.36
Epithelial hyperplasia	2	0.64	5.12	Epithelial hyperplasia	6	0.65	3.70
Atrophy	1	0.05	0.48	Atrophy	2	0.33	2.59
Hyperkeratosis	0	0.00	0.00	Hyperkeratosis	2	0.33	2.59
Acanthosis	0	0.00	0.00	Acanthosis	1	0.23	2.42

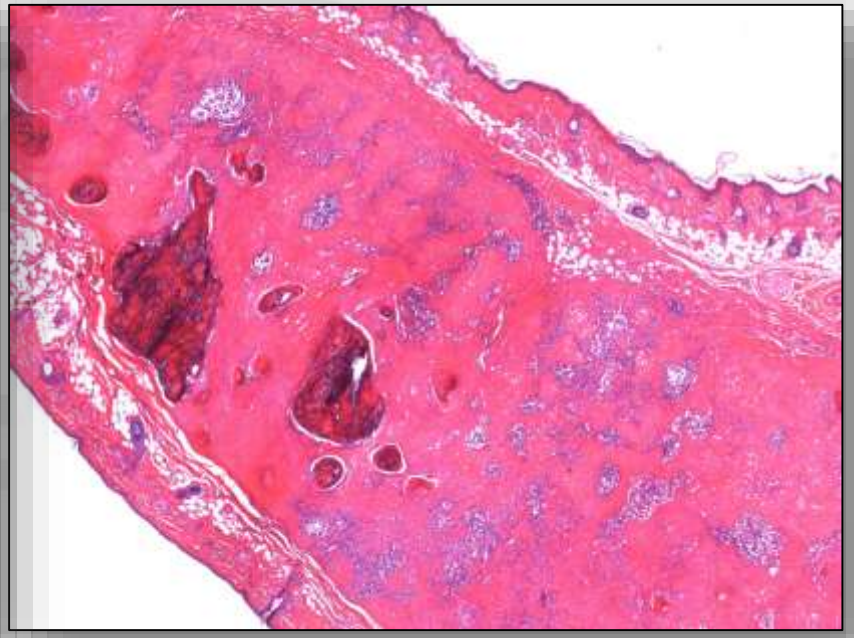
Non-Neoplastic lesions: Example, Rat. Males 26-W

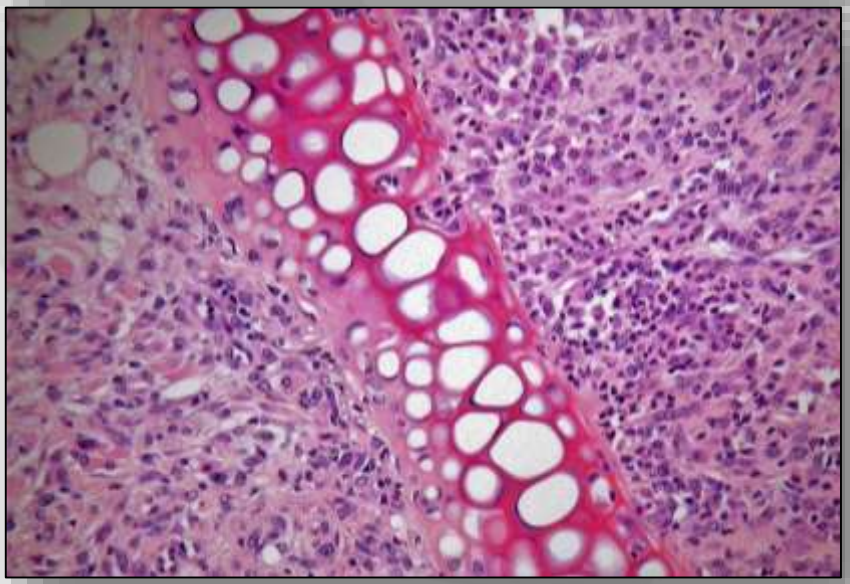
Male	Total n	Mean %	SD %	Male	Total n	Mean %	SD %
Numbers of rats examined	388			Numbers of rats examined	364		
	-				-		
Inclusion cyst	1	0.25	1.12	Inclusion cyst	0	0.00	0.00
Crust	0	0.00	0.00	Crust	1	0.26	1.15
Mononuclear cell foci	1	0.24	1.06	Mononuclear cell foci	10	2.63	6.74
Scab/Ulceration	0	0.00	0.00	Scab/Ulceration	0	0.00	0.00
Parakeratosis	0	0.00	0.00	Parakeratosis	0	0.00	0.00
Acanthosis	0	0.00	0.00	Acanthosis	8	2.11	9.18
Intramuscular edema	0	0.00	0.00	Intramuscular edema	1	0.26	1.15
Adnexal atrophy	8	2.58	10.44	Adnexal atrophy	8	2.72	10.70
Auricular chondropatty	5	1.15	3.19	Auricular chondropatty	4	1.05	2.68
Inflammation	0	0.00	0.00	Inflammation	1	0.20	0.88
Epidermal hyperplasia	0	0.00	0.00	Epidermal hyperplasia	5	1.32	4.67
Dermal granuloma	2	0.50	2.24	Dermal granuloma	0	0.00	0.00

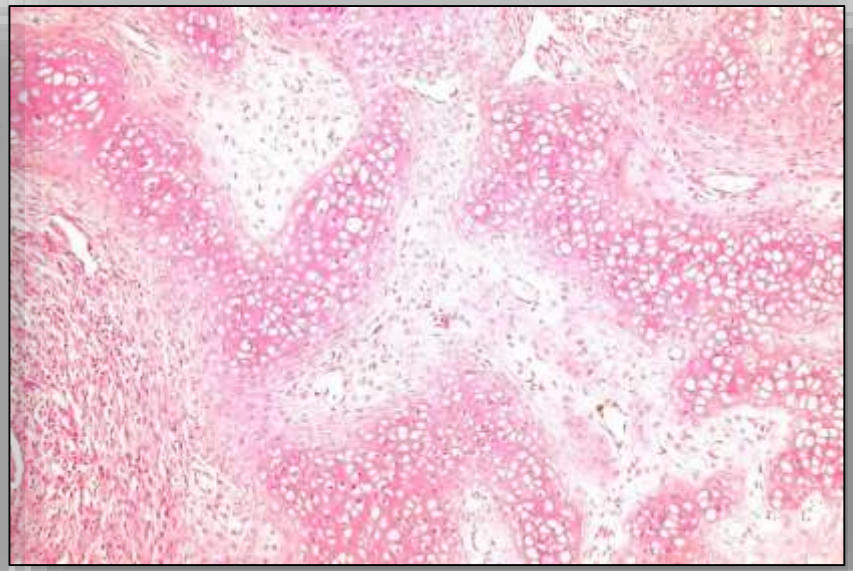
Non-Neoplastic lesions: Example, Rat. Males 104-W

Males	Total n	Mean %	SD %	Males	Total n	Mean %	SD %
Numbers of rats examined	3784			Numbers of rats examined	3784		
Auricular chondropathy	9	0.24	0.80	Granuloma	5	0.11	0.40
Epidermoid cyst ↑	64	1.78	2.01	Periarteritis/arteritis	1	0.04	0.27
Congestion	2	0.04	0.23	Folliculitis	19	0.44	2.33
Hemorrhage	2	0.04	0.23	Pododermatitis ↑	65	3.37	14.53
Edema	0	0.00	0.00	Inflammation	88	2.24	3.37
Alopecia	6	0.09	0.69	Fibrosis	19	0.45	1.11
Encrustation	3	0.11	0.61	Basal cell hyperplasia	0	0.00	0.00
Hair follicle crusting	2	0.06	0.40	Hyperkeratosis	51	1.60	7.45
Follicular keratosis	16	0.46	1.54	Intracutaneous keratosis	1	0.02	0.11
Atrophy of adnexum ↓	196	5.38	13.49	Parakeratosis	1	0.02	0.14
Osseous metaplasia	5	0.12	0.53	Acanthosis ↓	16	0.36	1.05
Mononuclear cell foci	12	0.39	1.27	Epidermal hyperplasia	1	0.02	0.14
Abscess ↑	23	0.66	1.23	Sebaceous hyperplasia	4	0.15	0.66
Fat necrosis	1	0.02	0.14	Cartilaginous hyperplasia	3	0.07	0.36
Necrosis	1	0.03	0.20	Hyperplasia ↓	41	0.85	4.37
Scab/ ulceration	5	0.13	0.68				

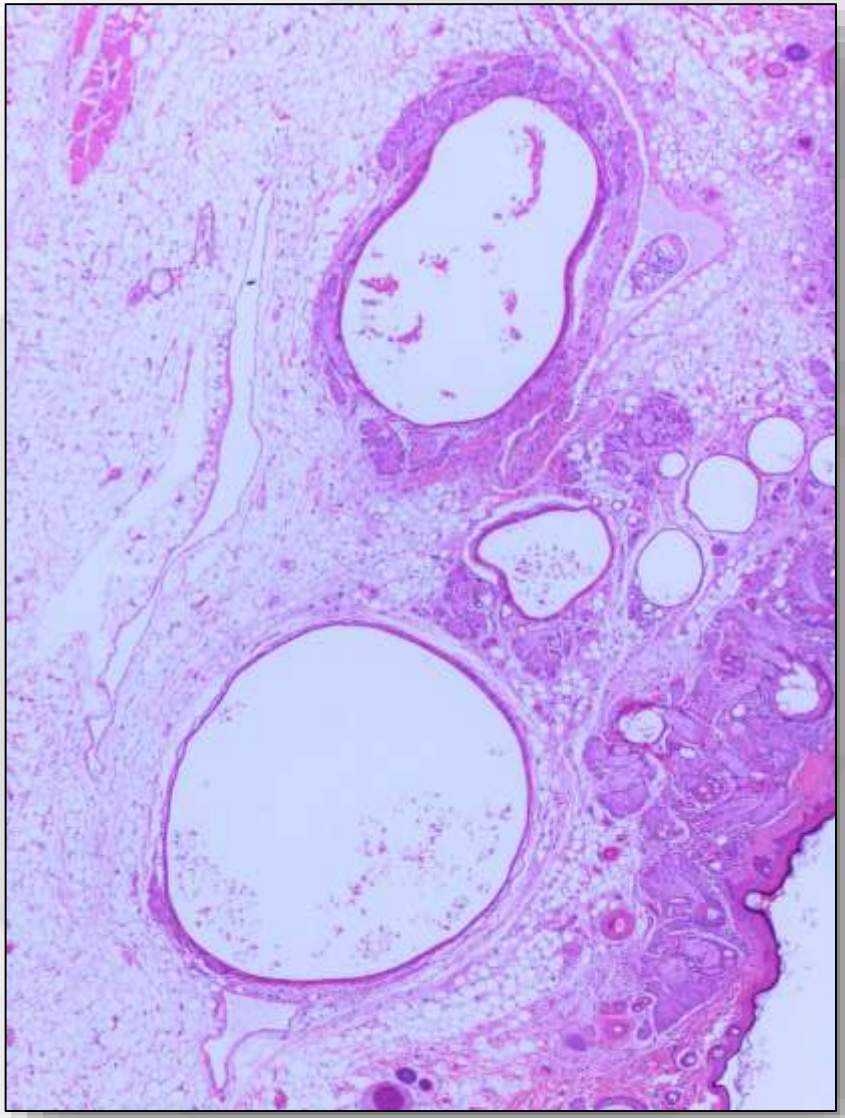
Auricular chondropathy: Rat

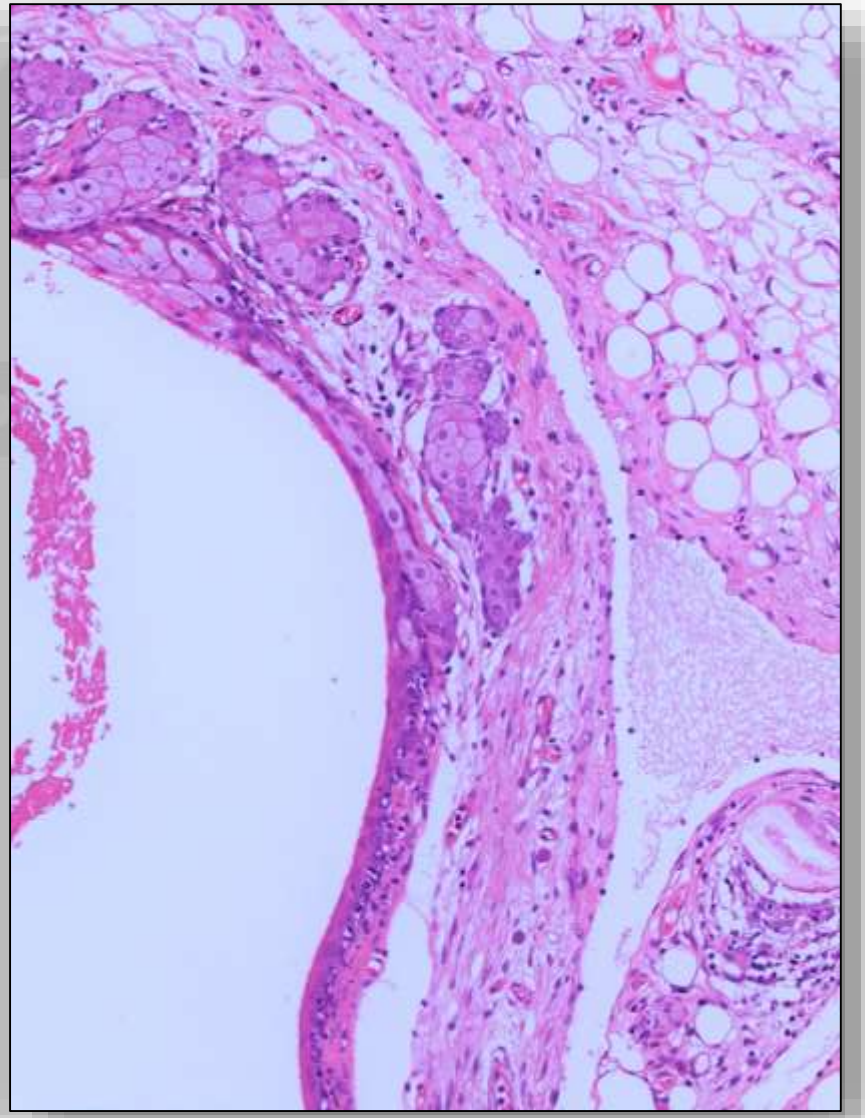




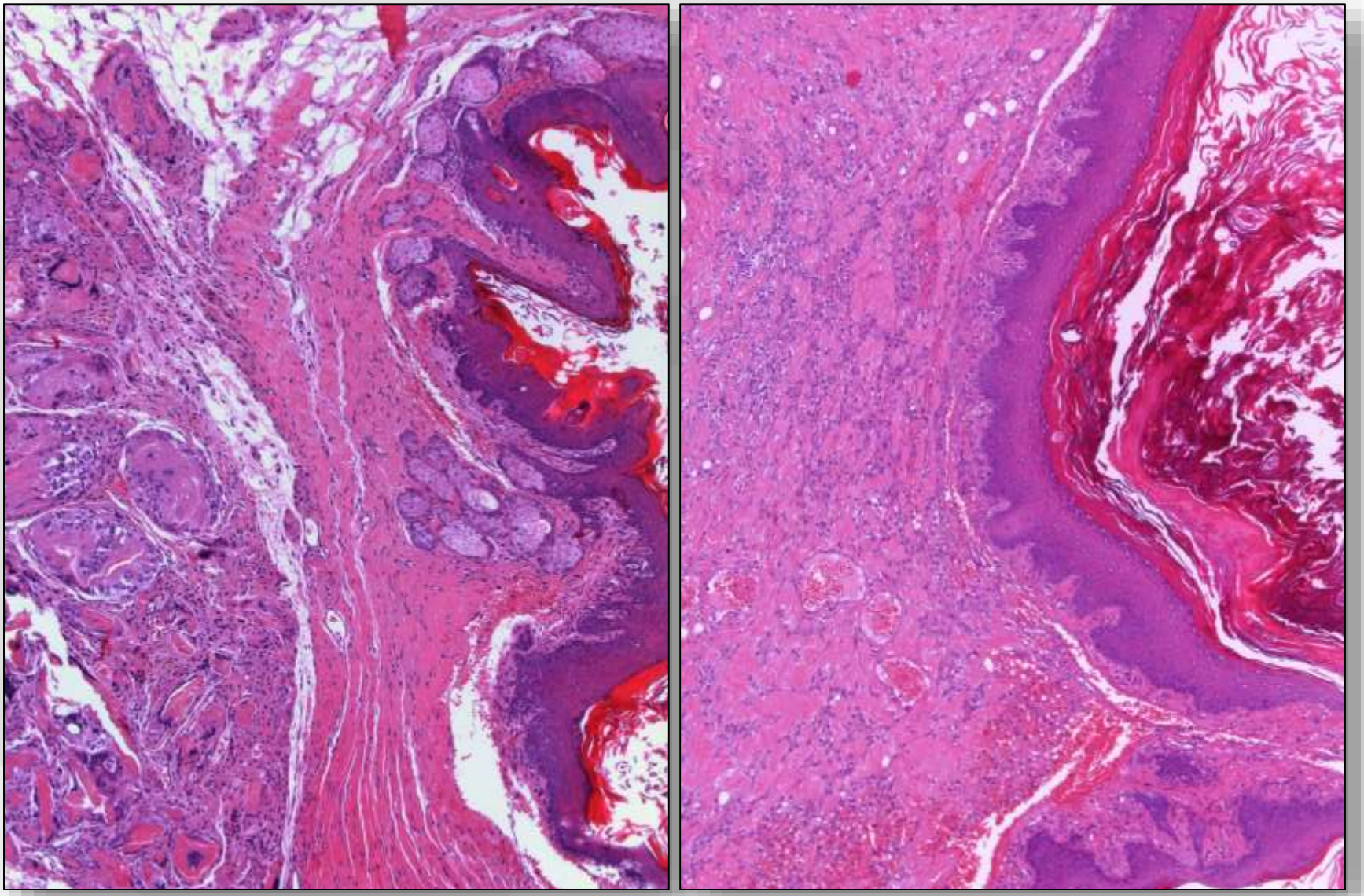


Follicular cyst: Rat





Epidermal hyperplasia, inflammation: Rat



Neoplastic Lesions: Rats

Male	Total n	Total %	SD %	Male	Total n	Total %	SD %
Numbers of rats examined	3725			Numbers of rats examined	3725		
Papilloma ↑	53 (vs 6)	1.42	4.69	Squamous cell ca	31	1.48	1.48
Keratocanthoma ↑	150 (vs 4)	4.03	6.48	Carcinoma, NOS	3	0.31	0.31
Adenoma (NOS)	0	0.00	0.00	Basal cell carcinoma	9	1.38	1.38
Sebaceous ad. ↓	14 (vs 4)	0.38	0.76	Fibrosarcoma	16	1.47	1.47
Tricholemmoma	3	0.08	0.36	Fibroliposarcoma	1	0.14	0.14
Trichoepithelioma	4	0.11	0.60	Leiomyosarcoma	0	0.00	0.00
Trichofolliculoma	0	0.00	0.00	Liposarcoma	5	0.40	0.40
Basal cell tumor b	9	0.24	0.93	Hemangiosarcoma ↑	14 (vs 1)	0.70	0.70
Granular cell t (b)	0	0.00	0.00	Cystic sarcoma	5	0.52	0.52
Fibroma ↑	135 (vs 38)	3.62	13.58	Sarcoma, NOS ↑	24 vs 4)	2.84	2.84
Lipoma ↑	34 (vs 17)	0.91	3.03	Histiocytic sarcoma	4	0.45	0.45
Leiomyoma	0	0.00	0.00	Benign basal cell t.	1	0.76	0.76
Hemangioma	9	0.24	0.91	Neural crest tumor	1	0.13	0.13
Schwannoma (b)	5	0.13	0.47	Osteosarcoma	1	0.14	0.14
Schwannoma (m) ↑	19 (vs 3)	0.51	1.04	Rhabdomyosarcoma	1	0.33	0.11
Carcinoma in situ	2	0.05	0.28	Zymbal gl. adenoma	2	036	0.68
Sebaceous ca	6	0.16	0.44	Zymbal gland ca.	3	0.55	0.770.00
				Metastatic ca	1	0.03	0.28

Neoplasms, Rat, Strain Differences

Strain/ Sex	F344		Hsd:SD		Crl:CD(SD)		Crl:WI(Han)		RccHan™: WIST	
	M	F	M	F	M	F	M	F	M	F
Number of Rats	1298	1250	120	120	2146	2342	1217	1217	3725	3719
Keratoacanthoma	5.16	0.56	16.67	0.83	2.42	0.34	1.89	0.41	4.03	0.11
Squamous papilloma	0.77	0.16	0.83	0.83	1.58	0.13	0.49	0	1.42	0.16
Basal cell adenoma	1.16	0.4	4.17	0	0.51	0.13	0.33	0.41	0.24	0.11
Basal cell carcinoma	0.85	0.16	1.67	0	0.33	0.13	0.25	0.25	0.24	0.11
Sebaceous gland adenoma	0.54	0.08	0.83	0.83	0.61	0	0.08	0	0.38	0.11
Hemangioma	0.08	0	0	0	0.14	0.73	0.08	0	0.24	0.03
Fibroma	8.71	2.0	8.33	2.5	4.01	0.60	0.41	0	3.62	1.02
Fibrosarcoma	1.31	0.32	0	0	1.40	0.34	0.08	0	0.43	0.43
Lipoma	1.23	0	0.83	0	2.19	1.07	0	0	0.91	0.46
Schwannoma, malignant	0.69	0.16	0	0	0.28	0.13	0	0	0.51	0.08
Squamous cell carcinoma	0.46	0.24	0.83	0	0.51	0.21	0.58	0	0.83	0.32
Sarcoma, NOS	0.69	0.16	0	0	0	0	0	0.08	0.64	0.11

Weber K. Differences in Types and Incidence of Neoplasms in Wistar Han and Sprague-Dawley Rats. Toxicol Pathol. 2017 Jan;45(1):64-75.

Non-Neoplastic Lesions: Mice

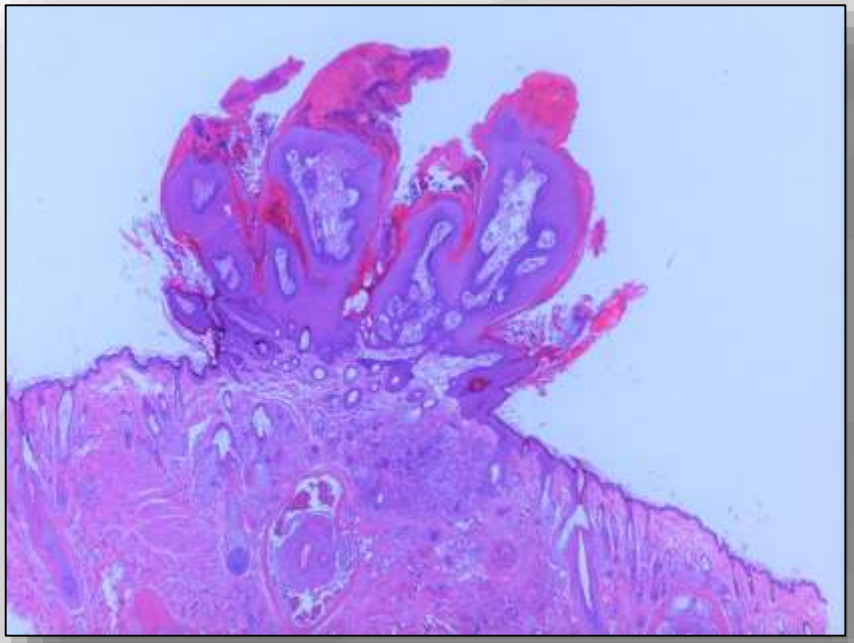
Neoplastic Lesions: CD-1 Mice

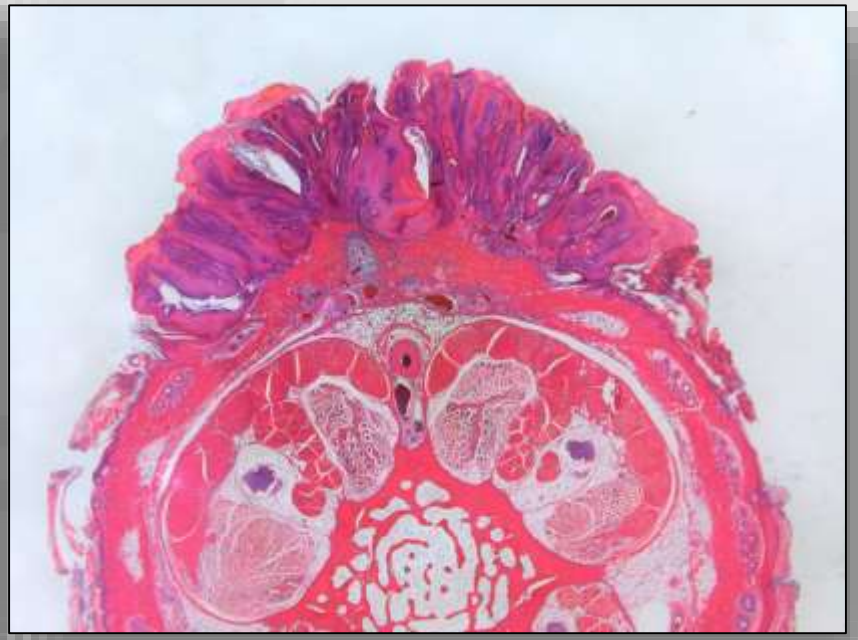
Males	Total n	Total %	SD %	Females	Total n	Total %	SD %
Numbers of mice examined	756			Numbers of mice examined	757		
Squamous papilloma	1	0.13	0.39	Squamous papilloma	2	0.26	1.22
Sebaceous adenoma	1	0.13	0.56	Sebaceous adenoma	0	0.00	0.00
Keratoacanthoma	0	0.00	0.00	Keratoacanthoma	1	0.13	0.29
Hemangioma	1	0.13	0.38	Hemangioma	0	0.00	0.00
Hair follicle tumor, benign	1	0.13	0.38	Hair follicle tumor, benign	0	0.00	0.00
Squamous carcinoma	0	0.00	0.00	Squamous carcinoma	2	0.26	0.59
Basal cell carcinoma	0	0.00	0.00	Basal cell carcinoma	2	0.26	0.66
Sebaceous carcinoma	1	0.13	0.56	Sebaceous carcinoma	0	0.00	0.00
Basoquamons carcinoma	0	0.00	0.00	Basoquamons carcinoma	2	0.26	0.66
Malignant schwannoma	0	0.00	0.00	Malignant schwannoma	1	0.13	0.38
Histiocytic sarcoma: skin	2	0.26	0.49	Histiocytic sarcoma: skin	0	0.00	0.00
Osteosarcoma	0	0.00	0.00	Osteosarcoma	1	0.13	0.56
Fibrosarcoma	0	0.00	0.00	Fibrosarcoma	2	0.26	0.44

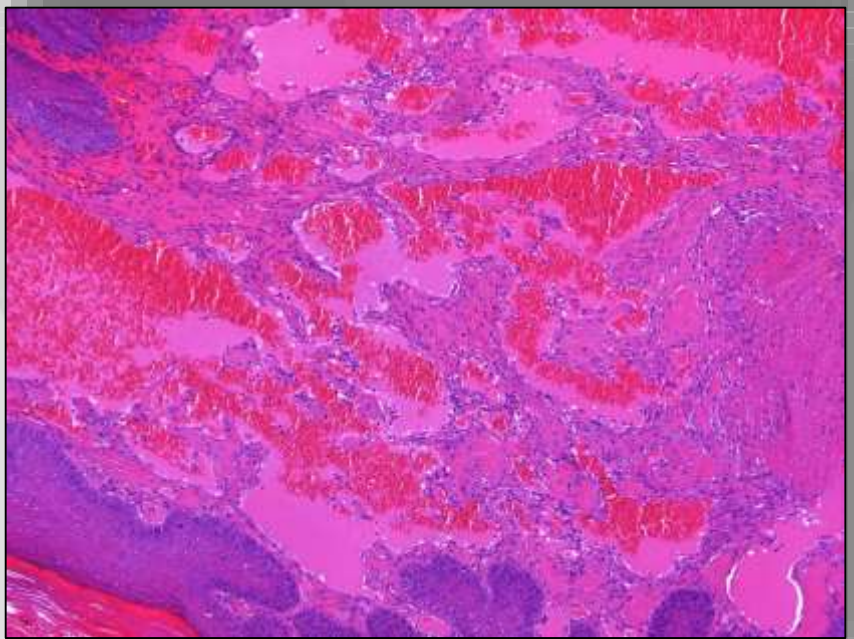
Neoplastic Lesions: NMRI Mice

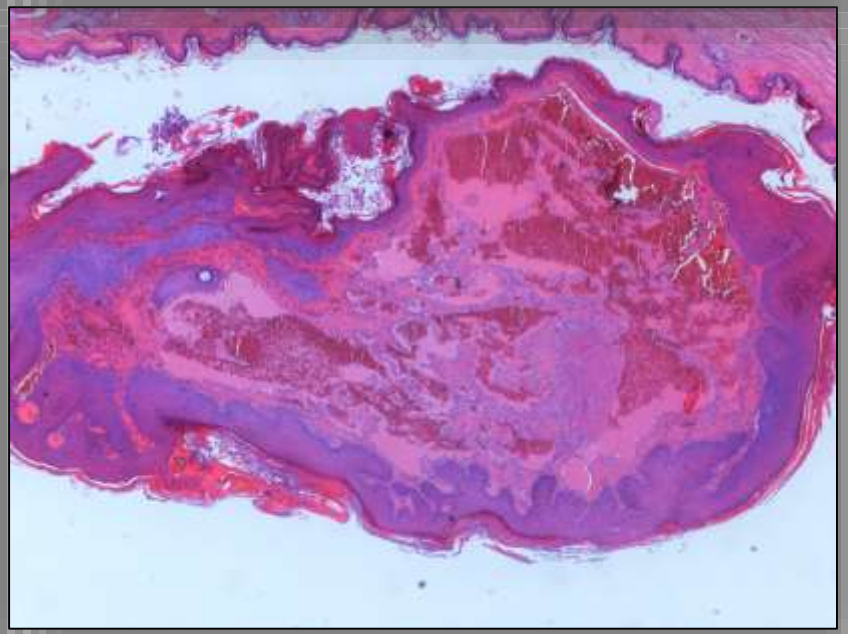
Males	Total n	Total %	SD %	Females	Total n	Total %	SD %
Numbers of mice examined	574			Numbers of mice examined	570		
Papilloma	1	0.17	0.67	Papilloma	1	0.18	0.67
Hemangioma	1	0.17	0.33	Hemangioma	0	0.00	0.00
Neurinoma, b	1	0.17	0.33	Neurinoma, b	1	0.18	0.34
Squamous cell carcinoma	1	0.17	0.68	Squamous cell carcinoma	1	0.18	0.67
Carcinoma (NOS)	1	0.17	0.67	Carcinoma (NOS)	0	0.00	0.00
Fibrosarcoma	2	0.35	1.36	Fibrosarcoma	0	0.00	0.00
Sarcoma (NOS)	0	0.00	0.00	Sarcoma (NOS)	1	0.18	0.34
Angiosarcoma	0	0.00	0.00	Angiosarcoma	1	0.18	0.67
Squamous pailloma	1	0.17	0.67	Squamous pailloma	2	0.35	0.55
Basal cell carcinoma	1	0.17	0.67	Basal cell carcinoma	1	0.18	0.27
Basosquam. Carcinoma	1	0.17	0.67	Basosquam. Carcinoma	1	0.18	0.27

Papilloma and Hemangioma in Papilloma

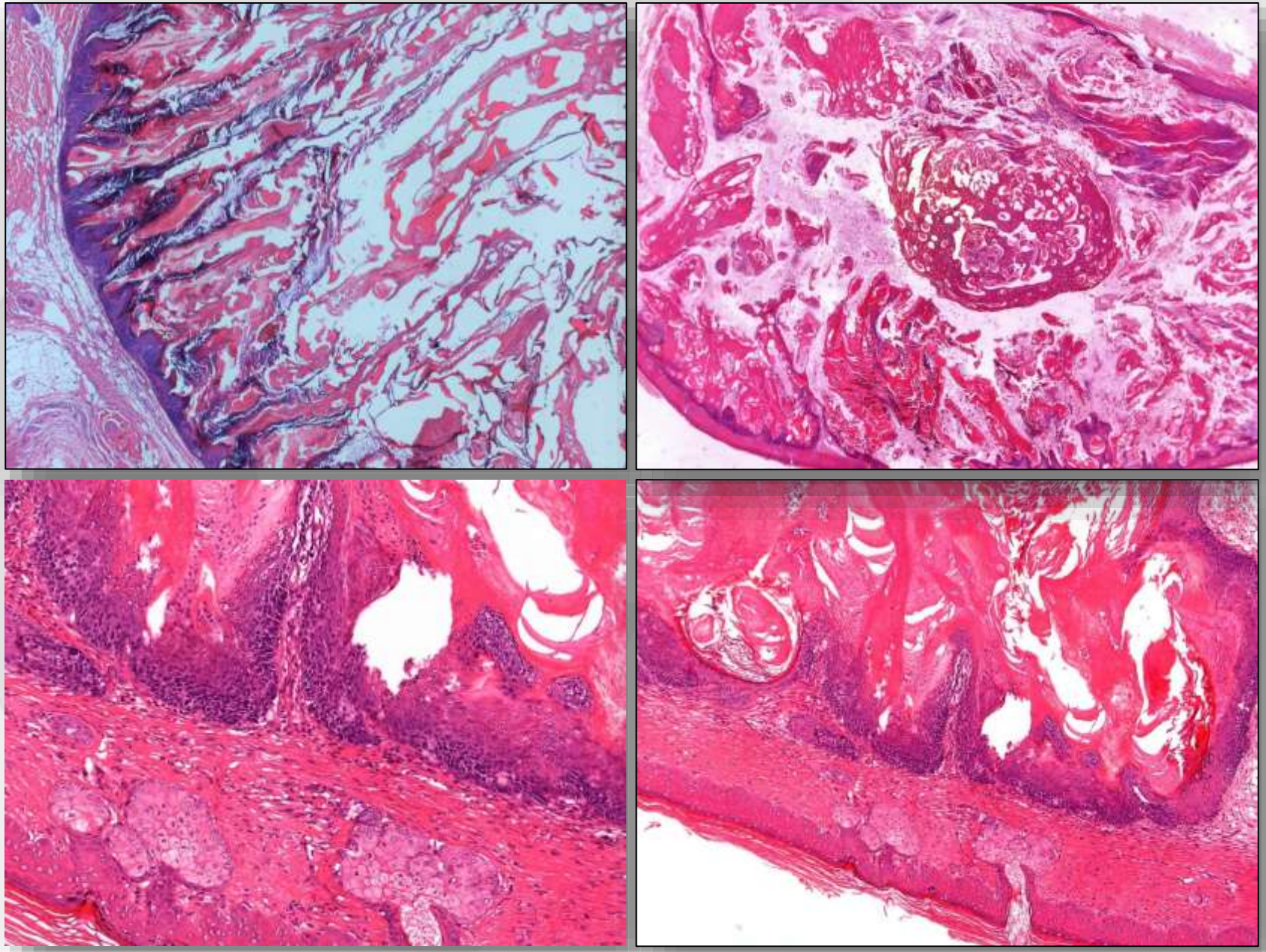




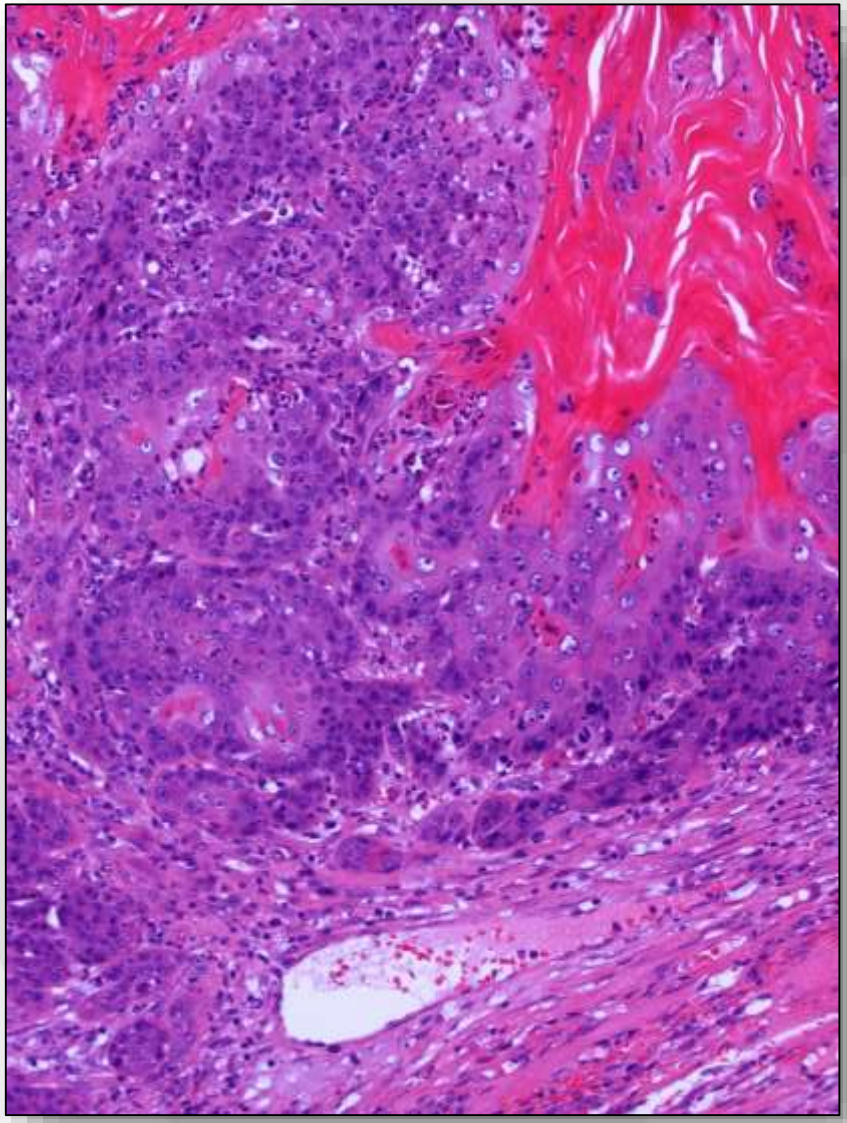


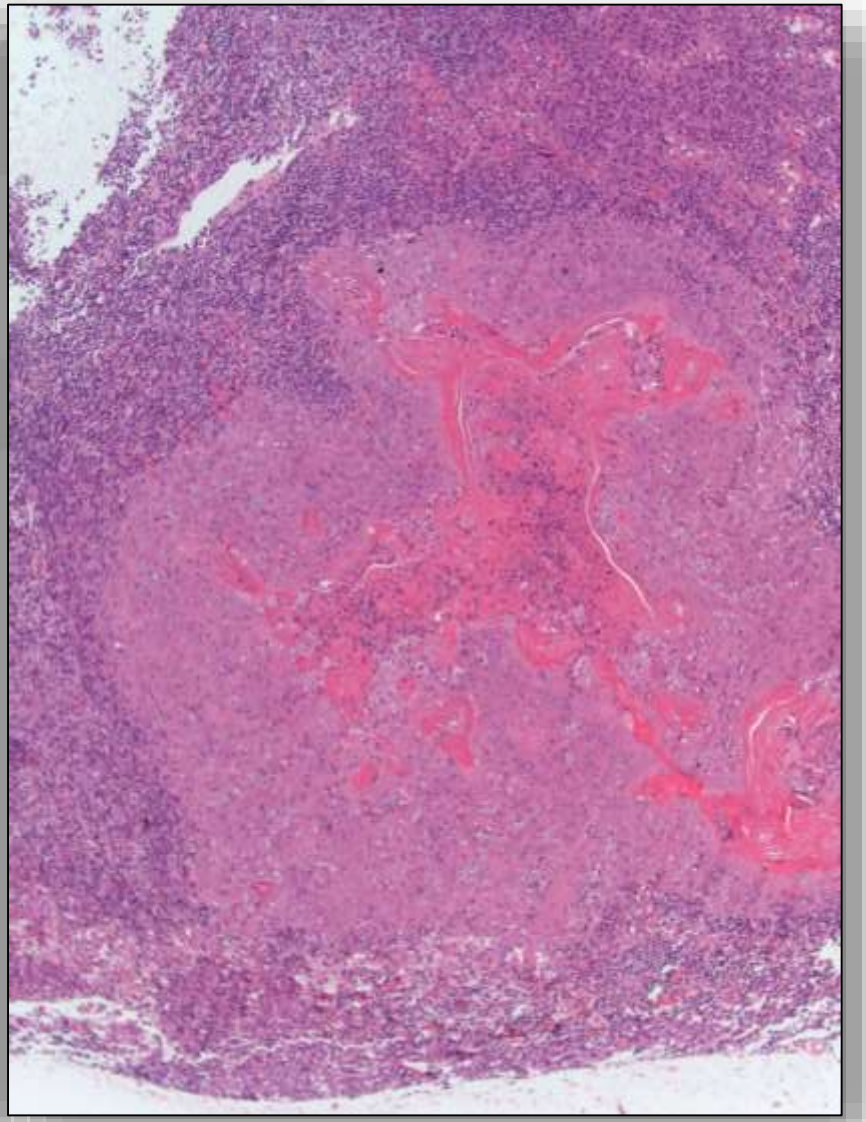


Keratoacanthoma

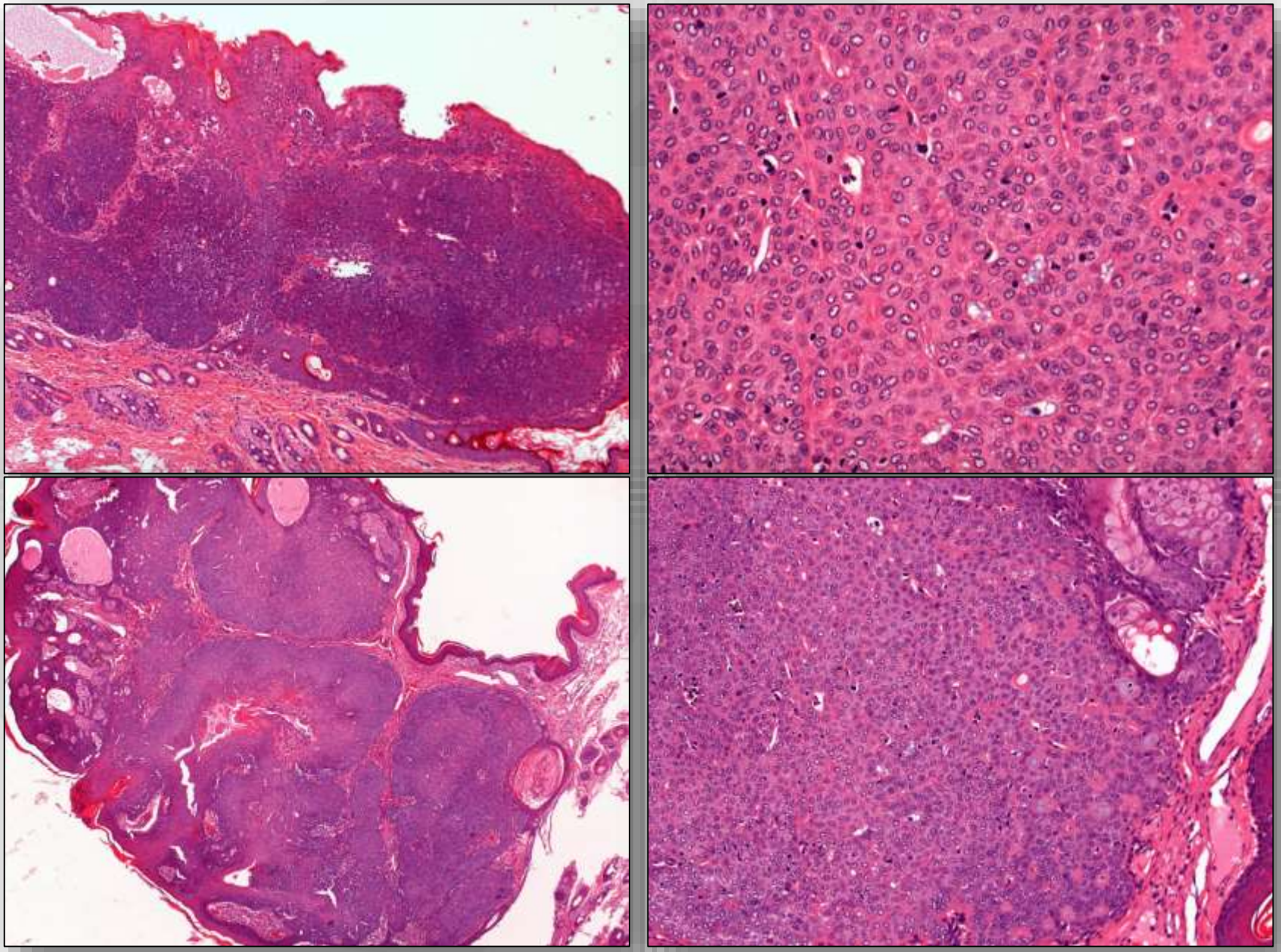


Squamous carcinoma

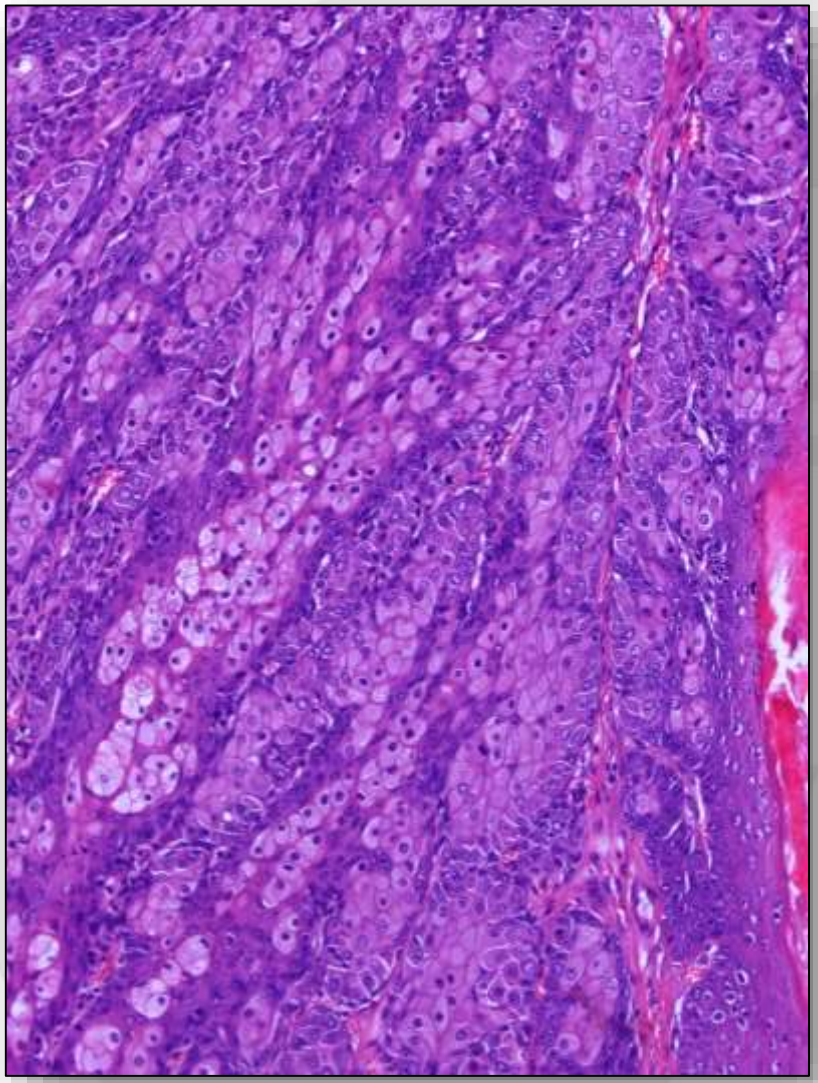


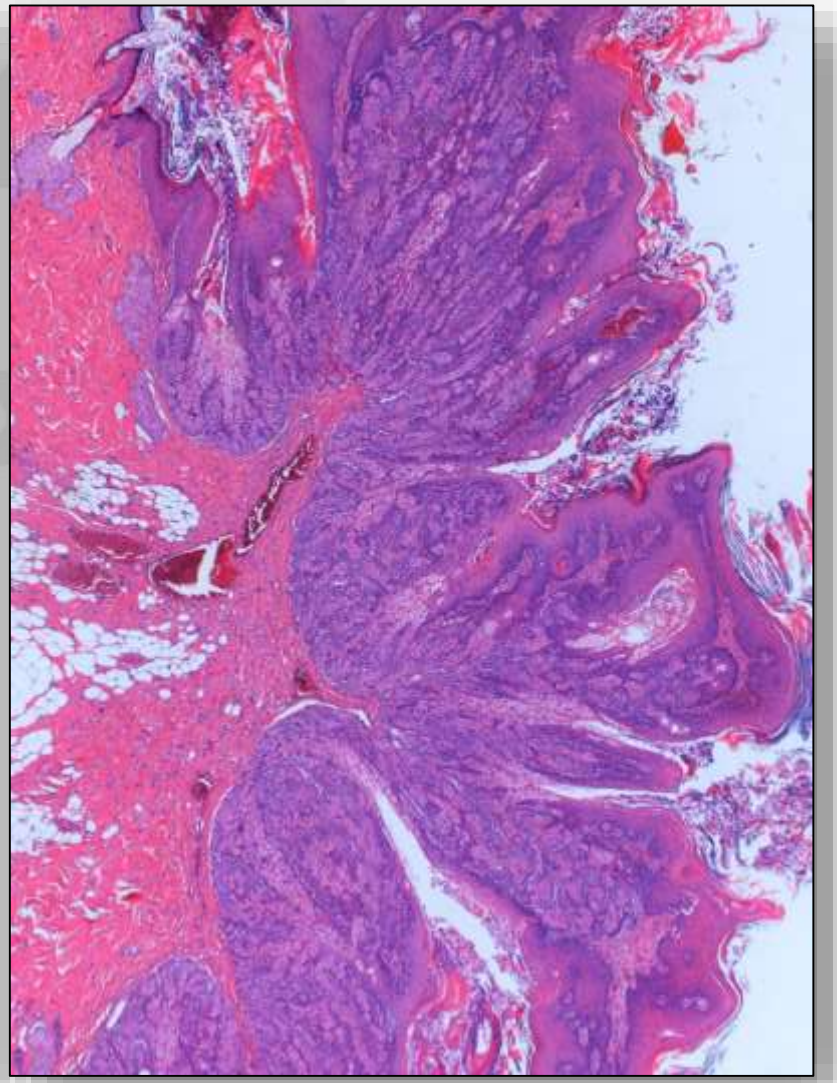


Basal cell tumor, benign

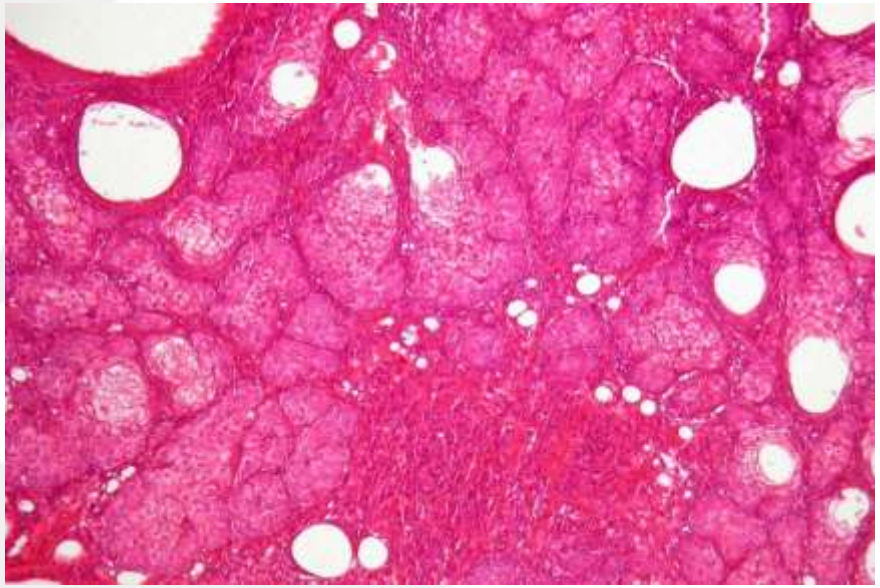


Sebaceous gland tumors

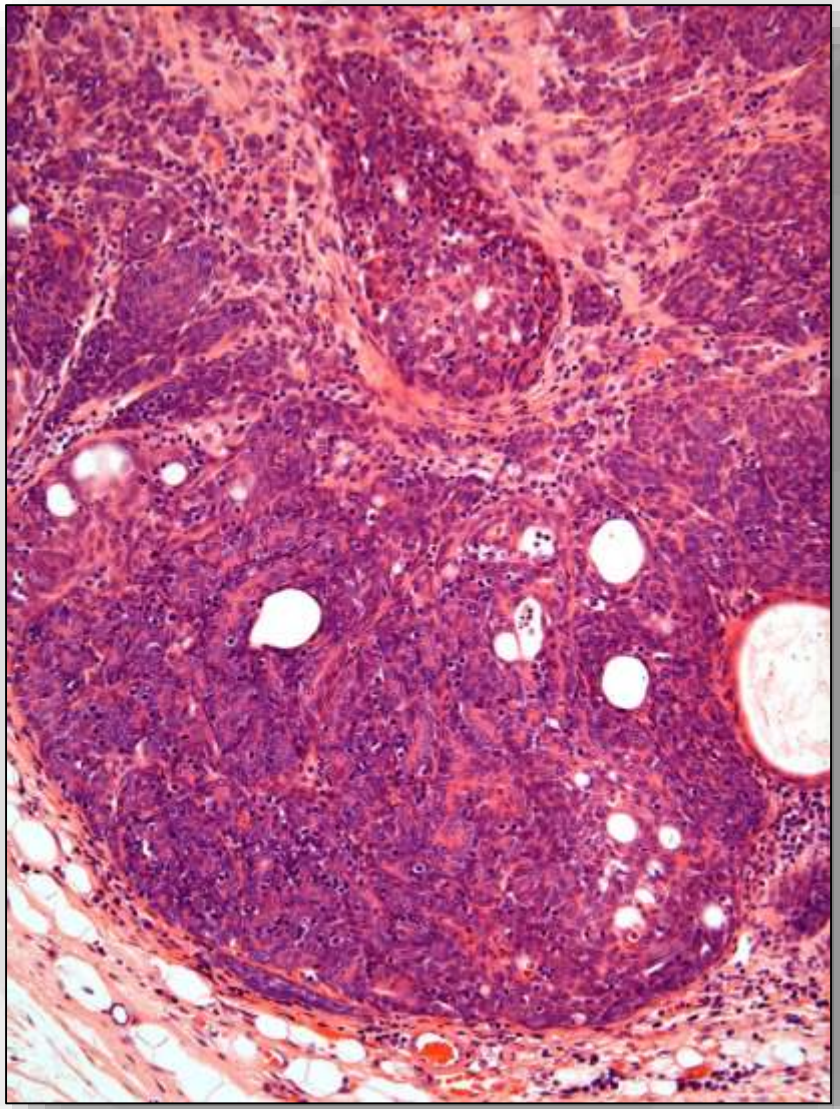


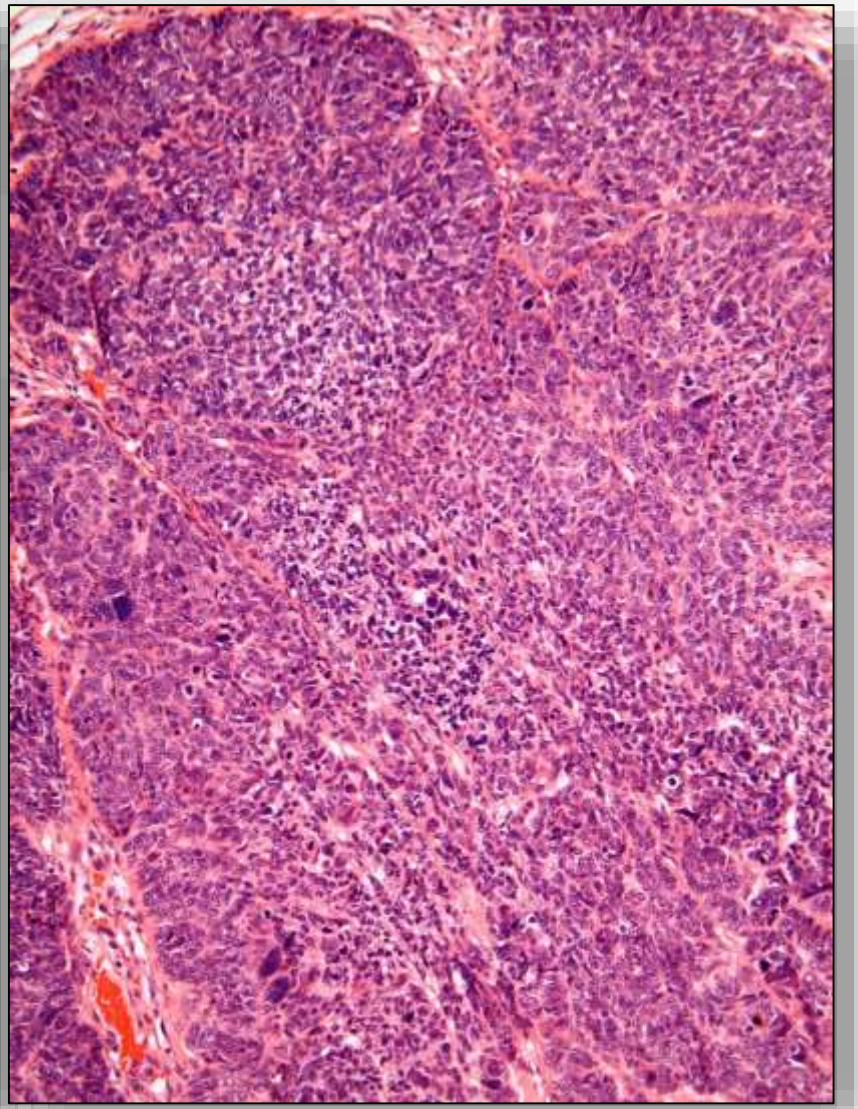


Sebaceous carcinoma

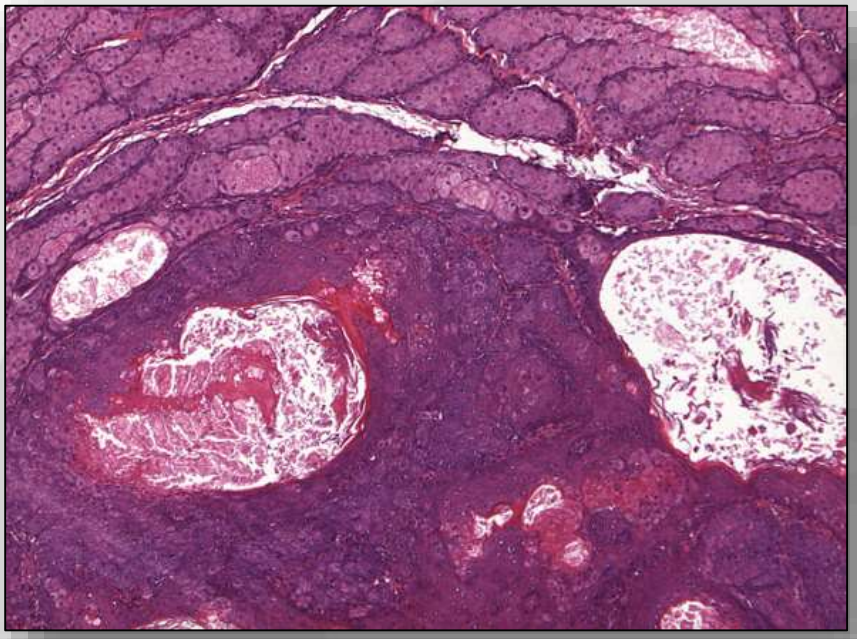


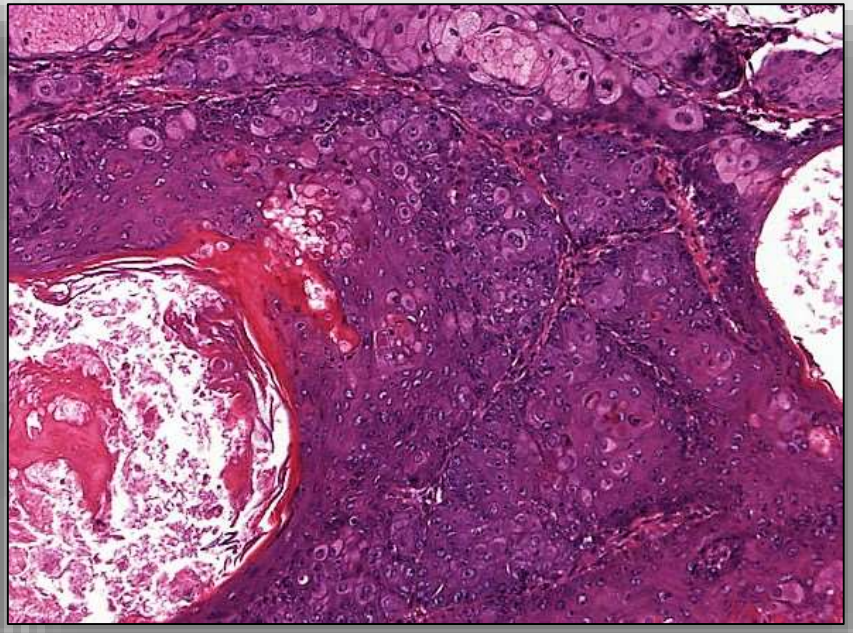
Basal cell carcinoma

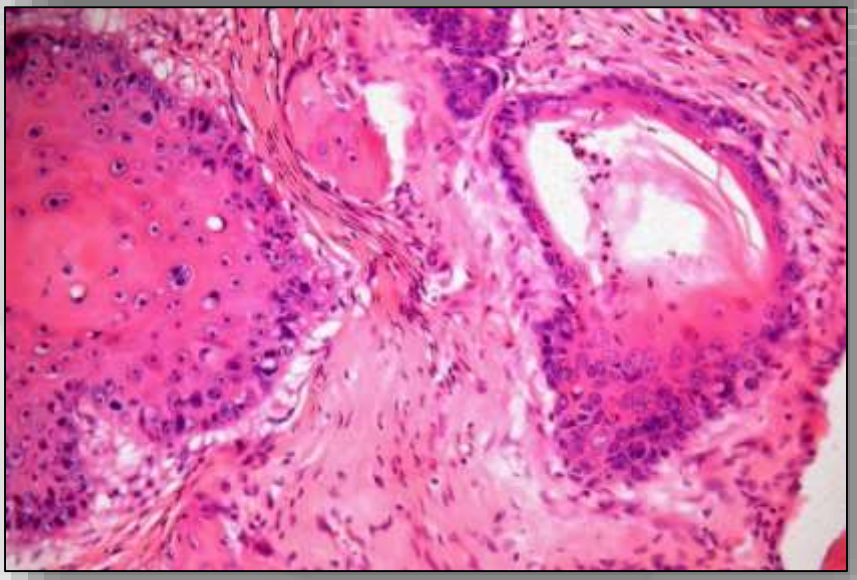


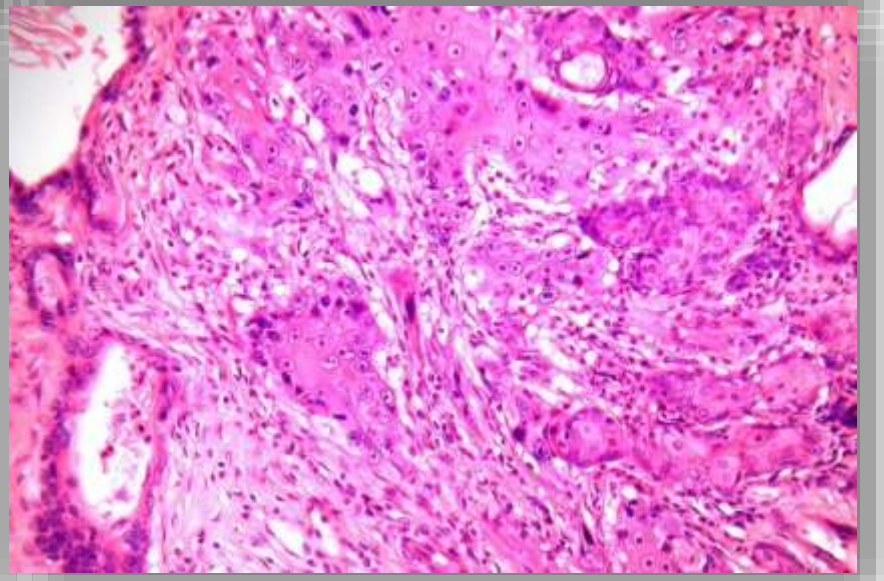


Zymbal gland tumor

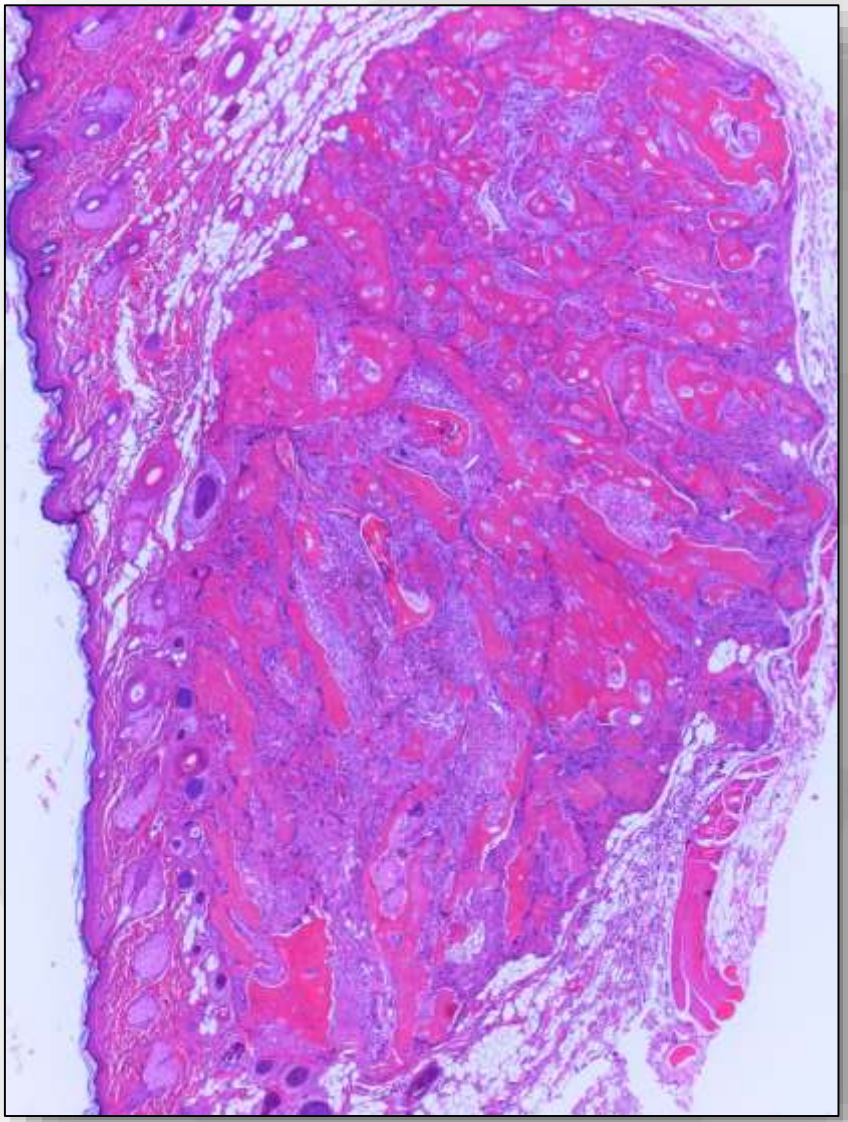


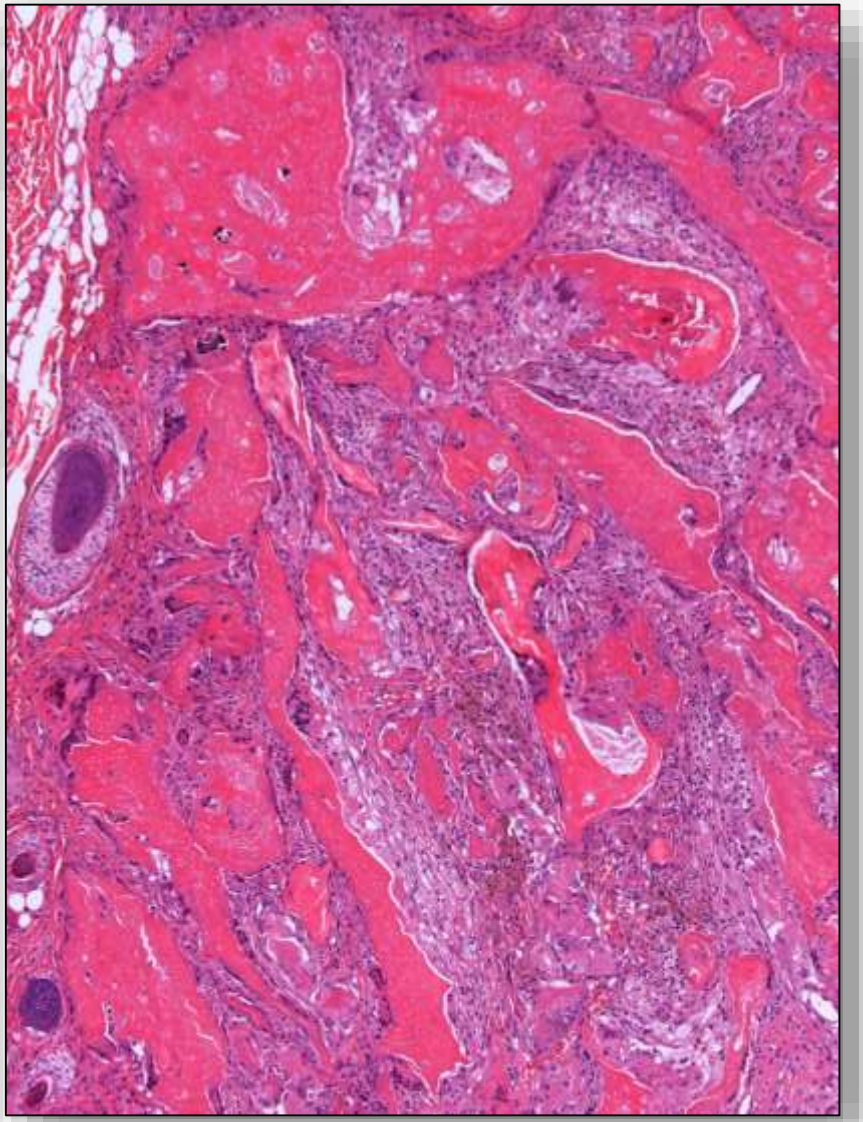






Hair follicle tumors: Pilomatricoma



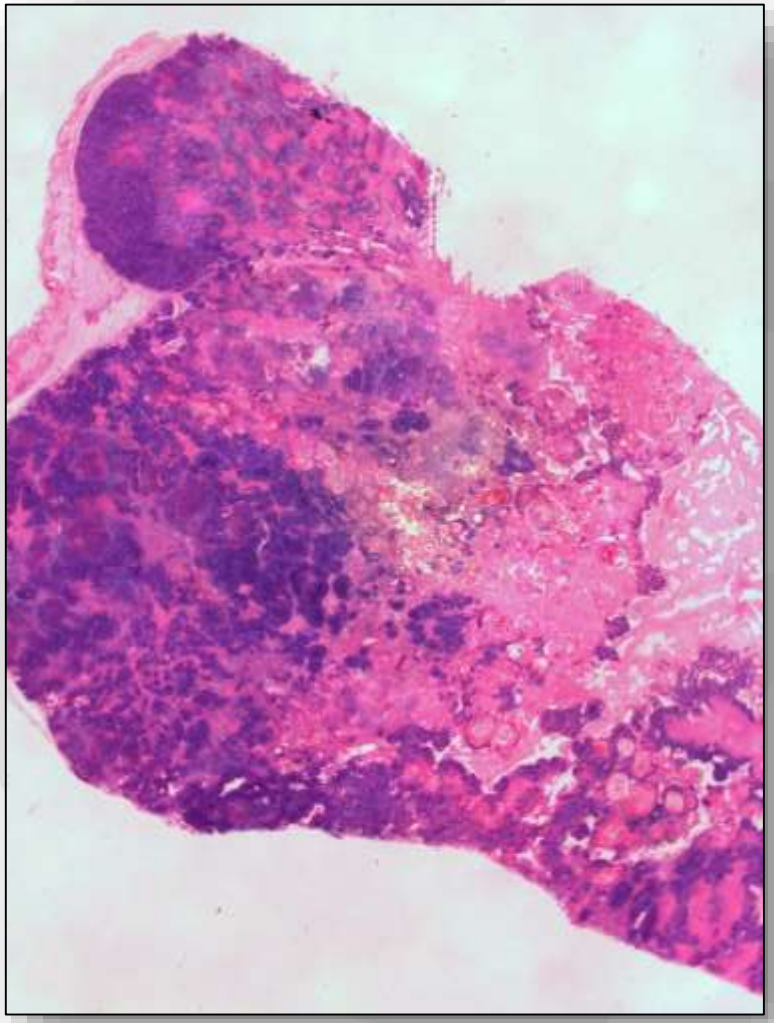


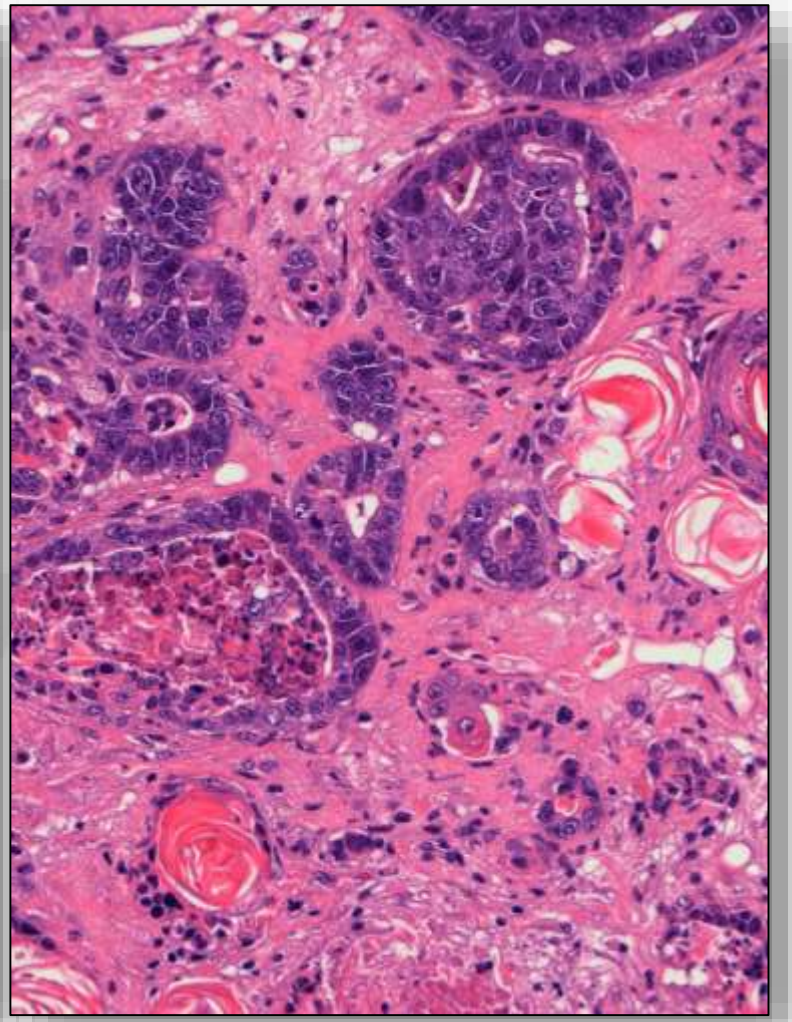
Calcifying hair follicle tumor (Malherbe)

Hair follicle tumors: Trichofolliculoma

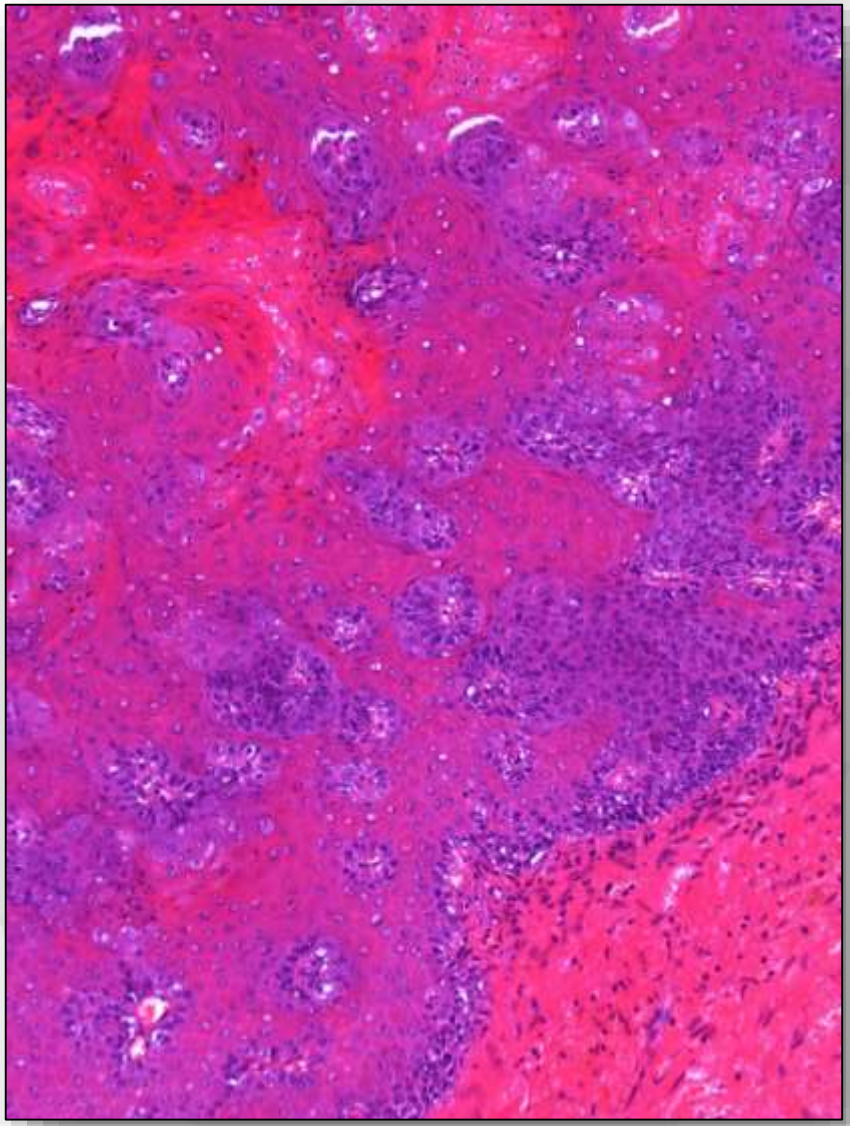
Tumor of the pilosebaceous unit (Mouse)

Is this a form of keratoacanthoma or this? A malignant squamo-basal cell tumor



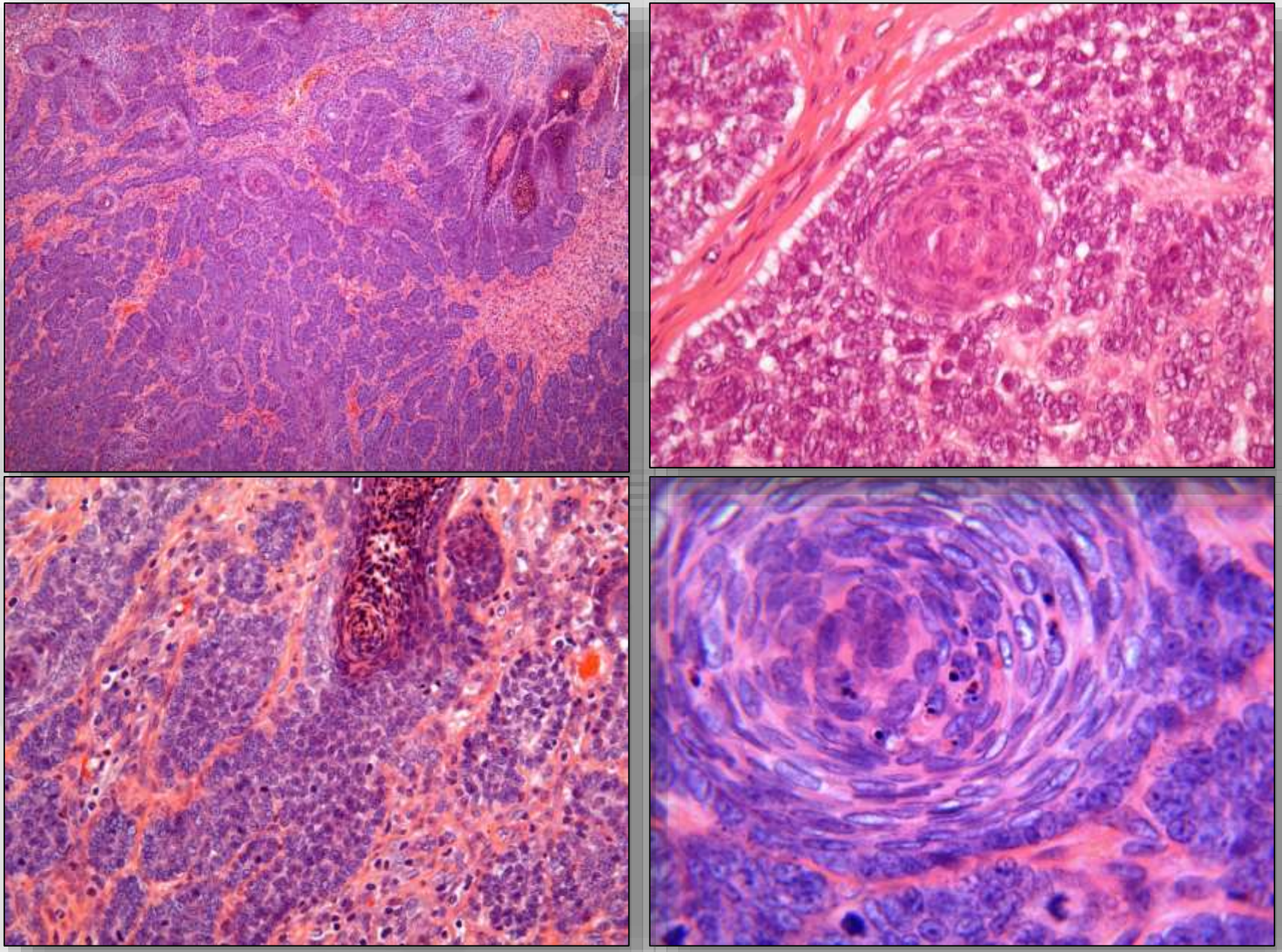


Hair follicle tumors: Tricholemmoma

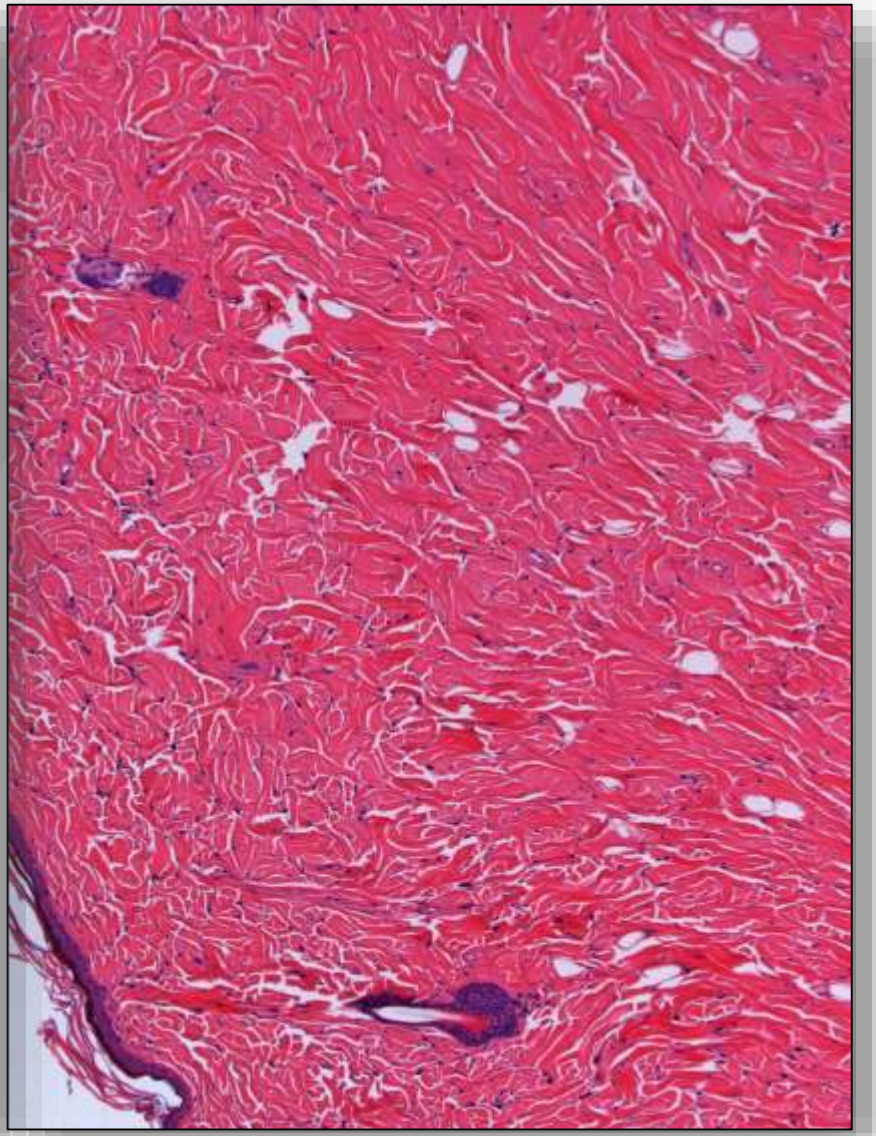


Outer root sheet hair follicle tumor

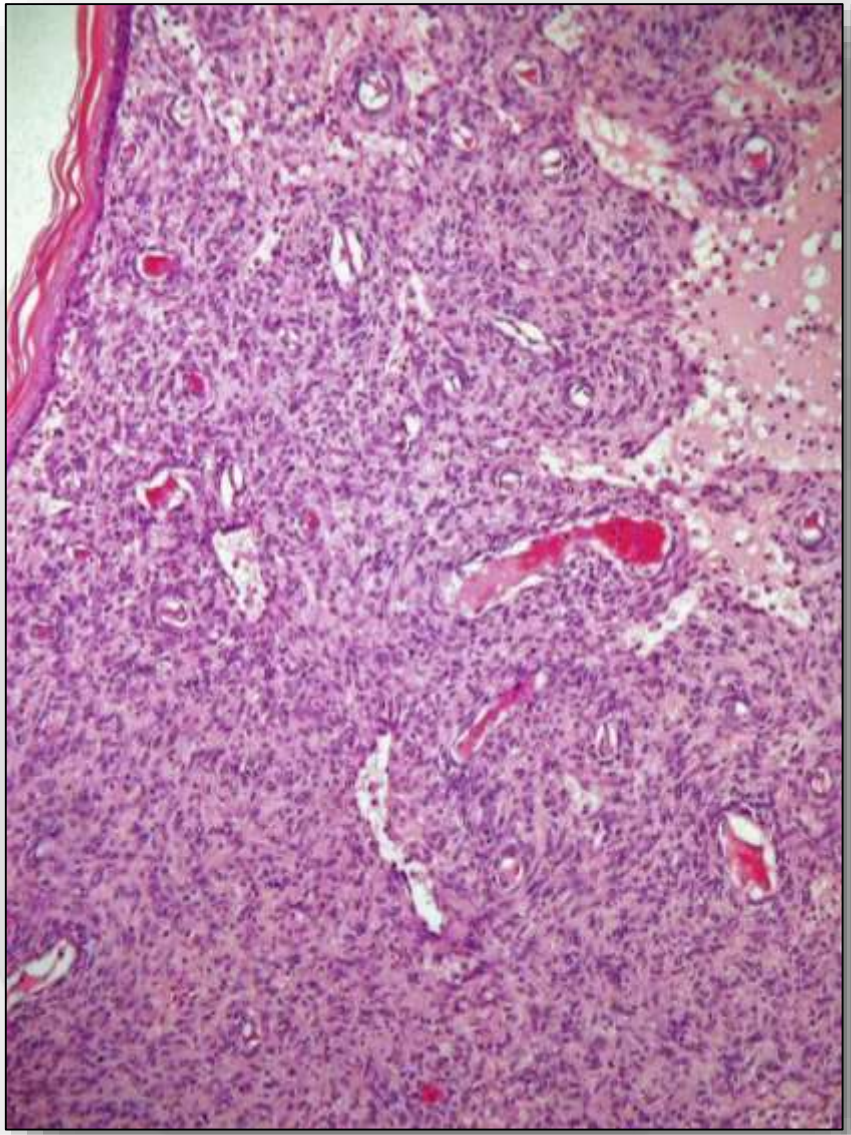
Hair follicle tumors: Trichoepithelioma

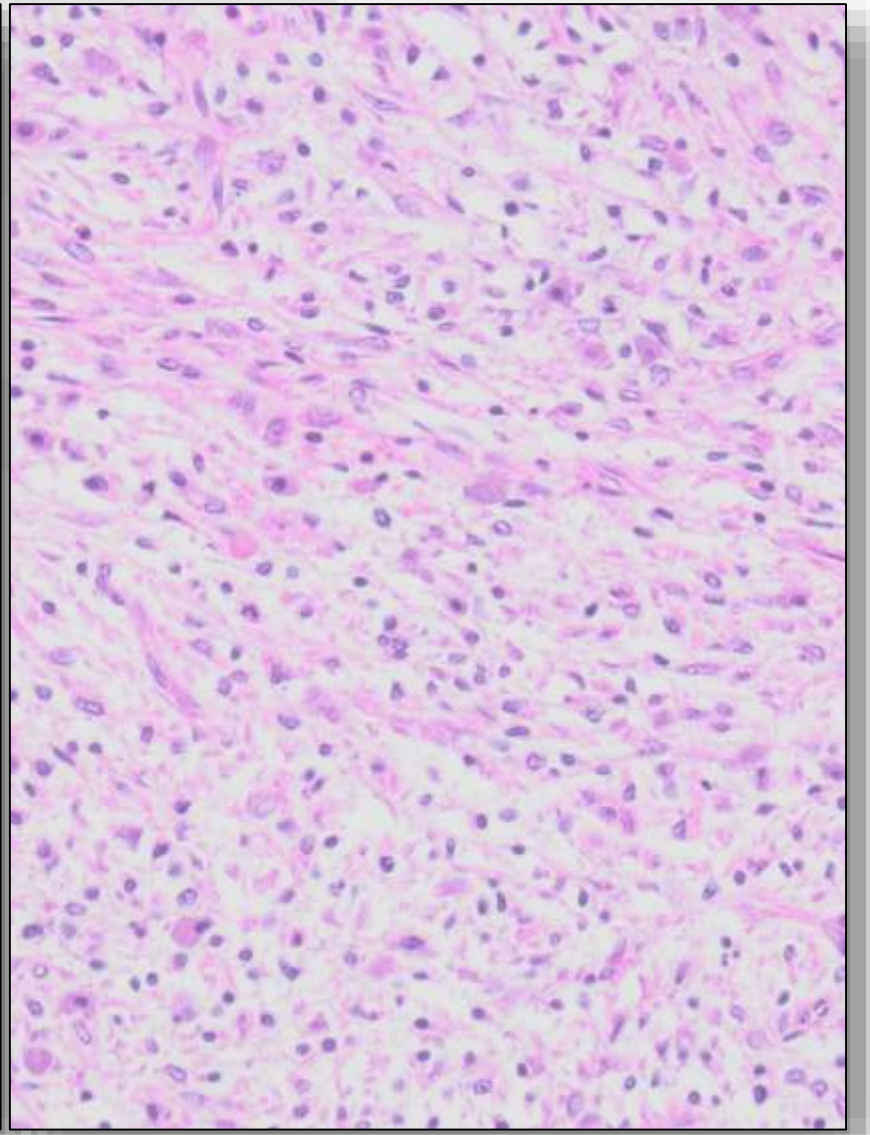


Fibroma

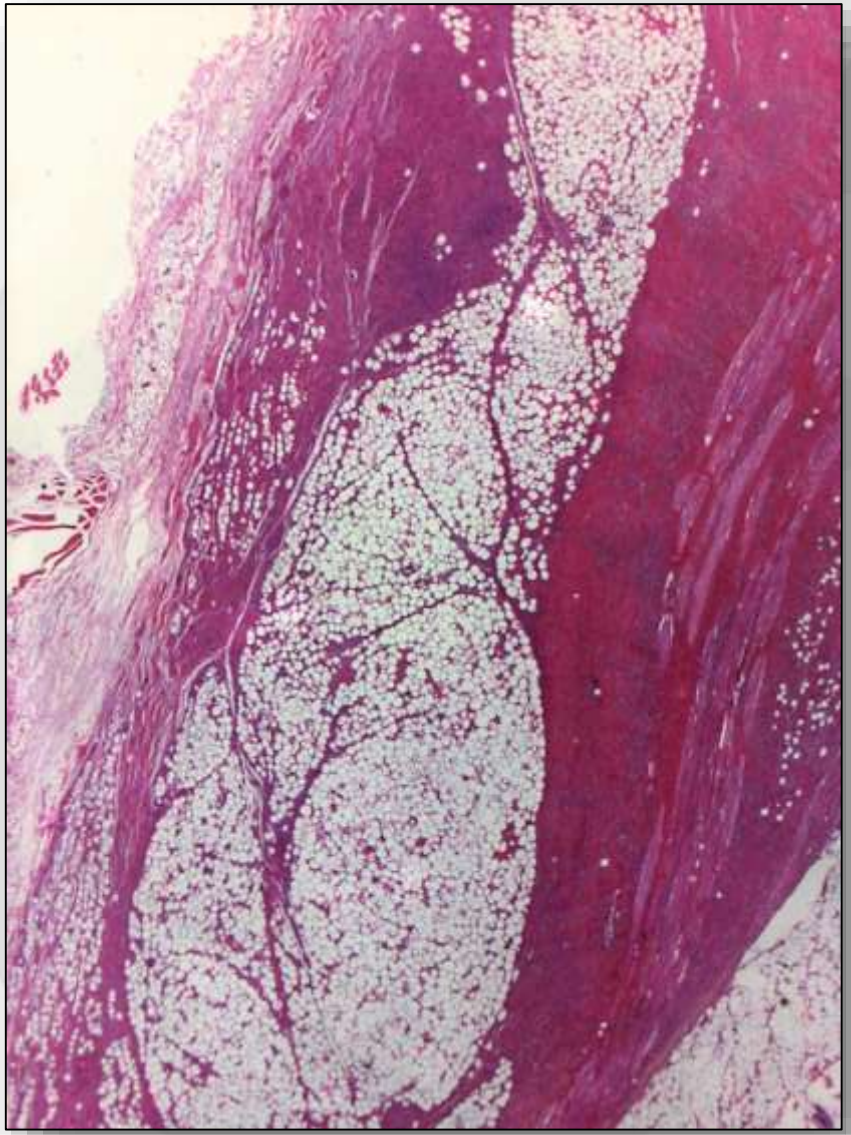


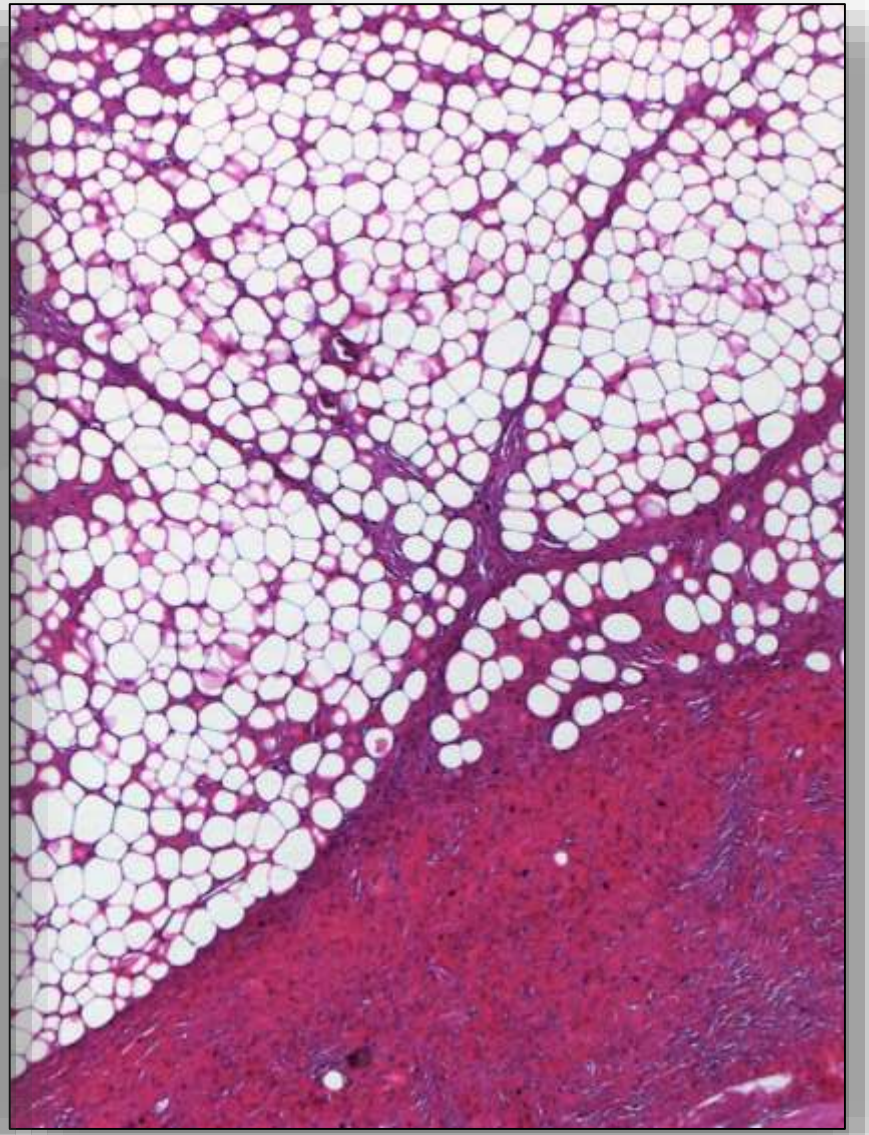
Fibrosarcoma



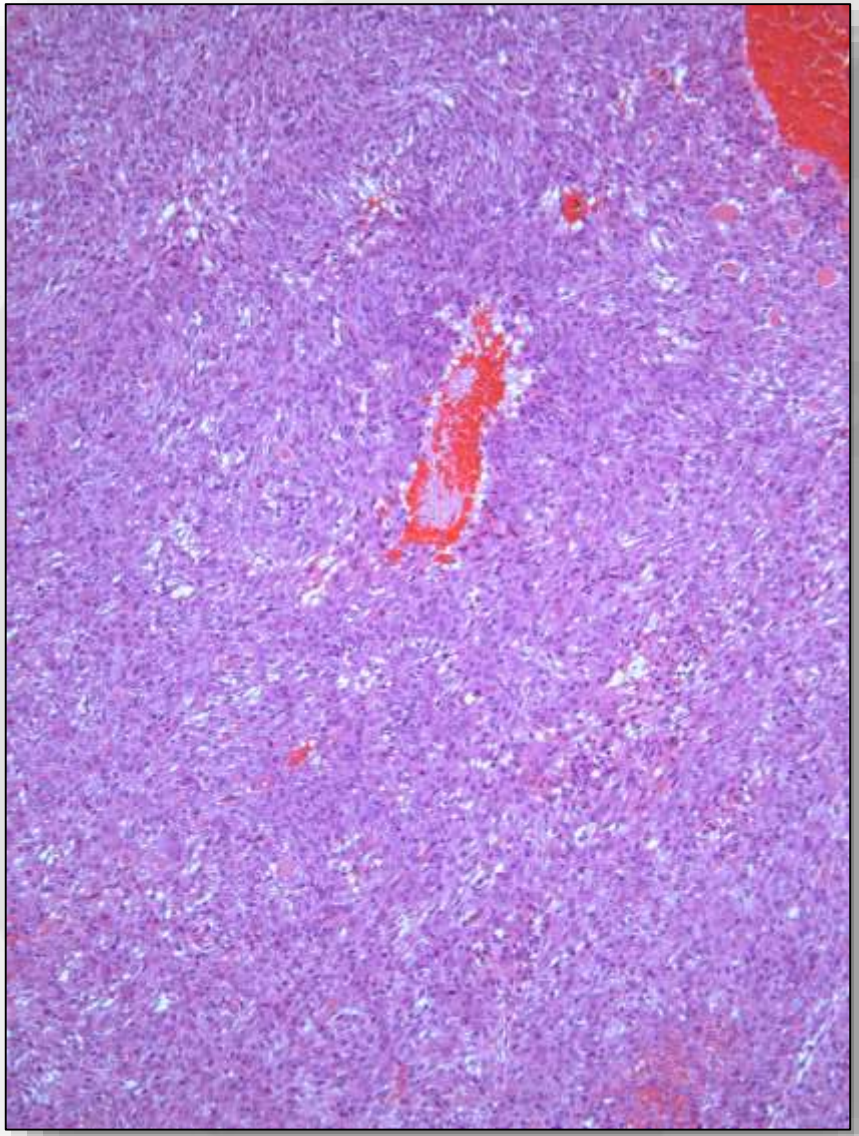


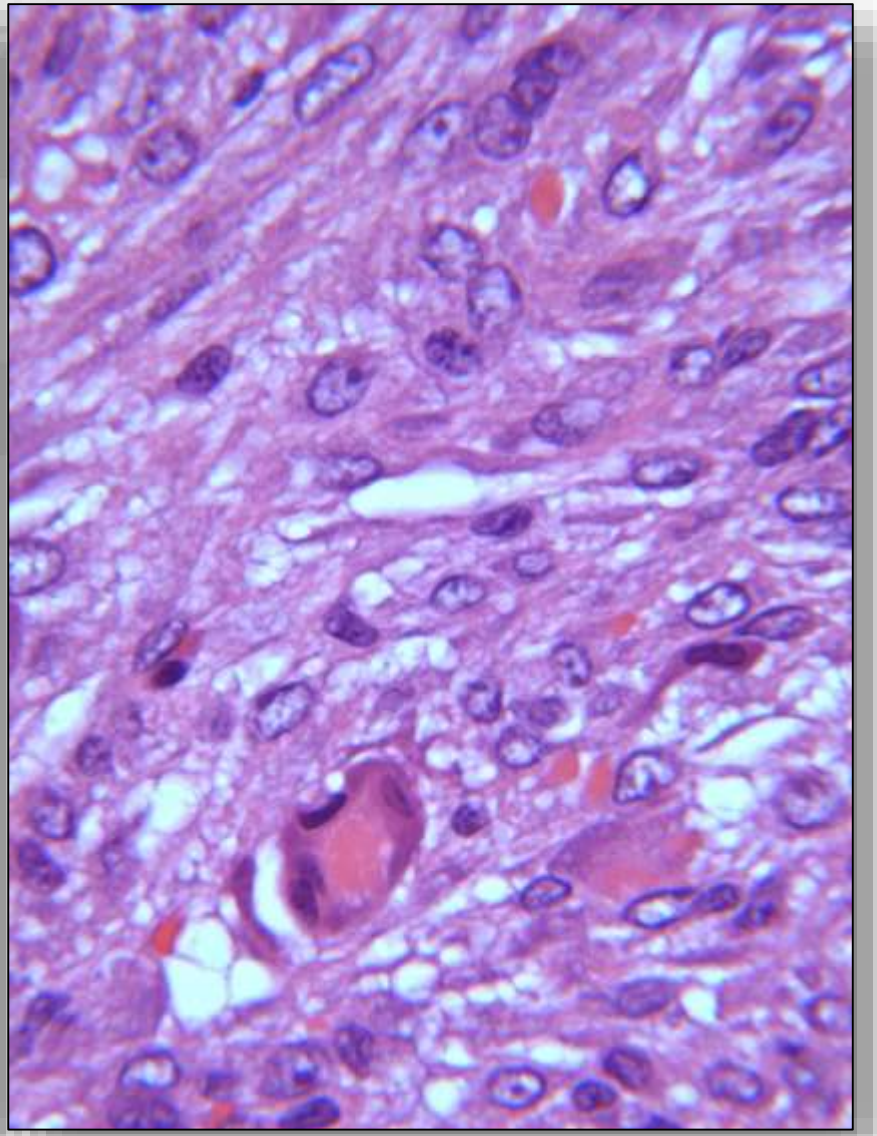
Fibrolipoma



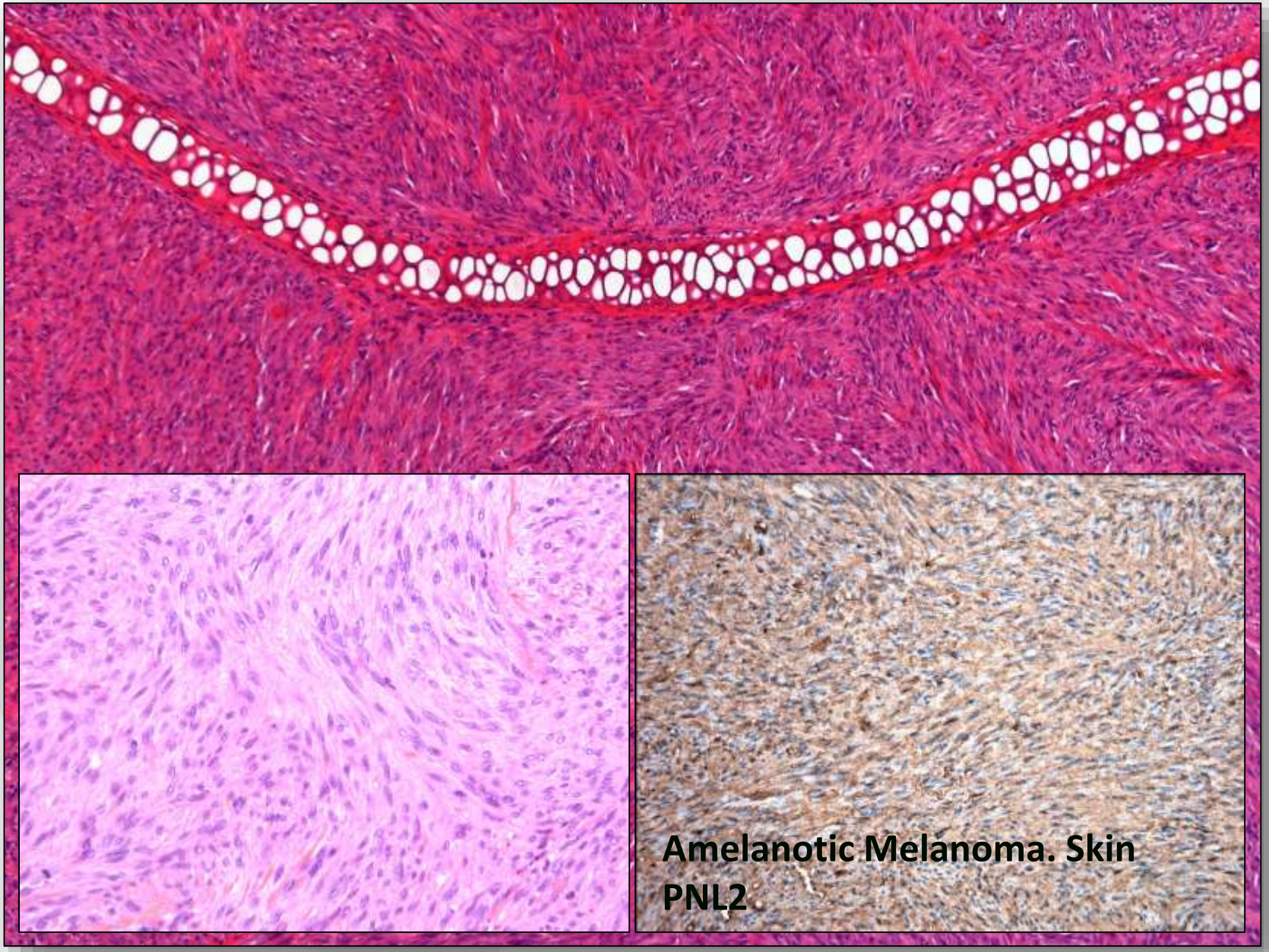


Rhabdomyosarcoma

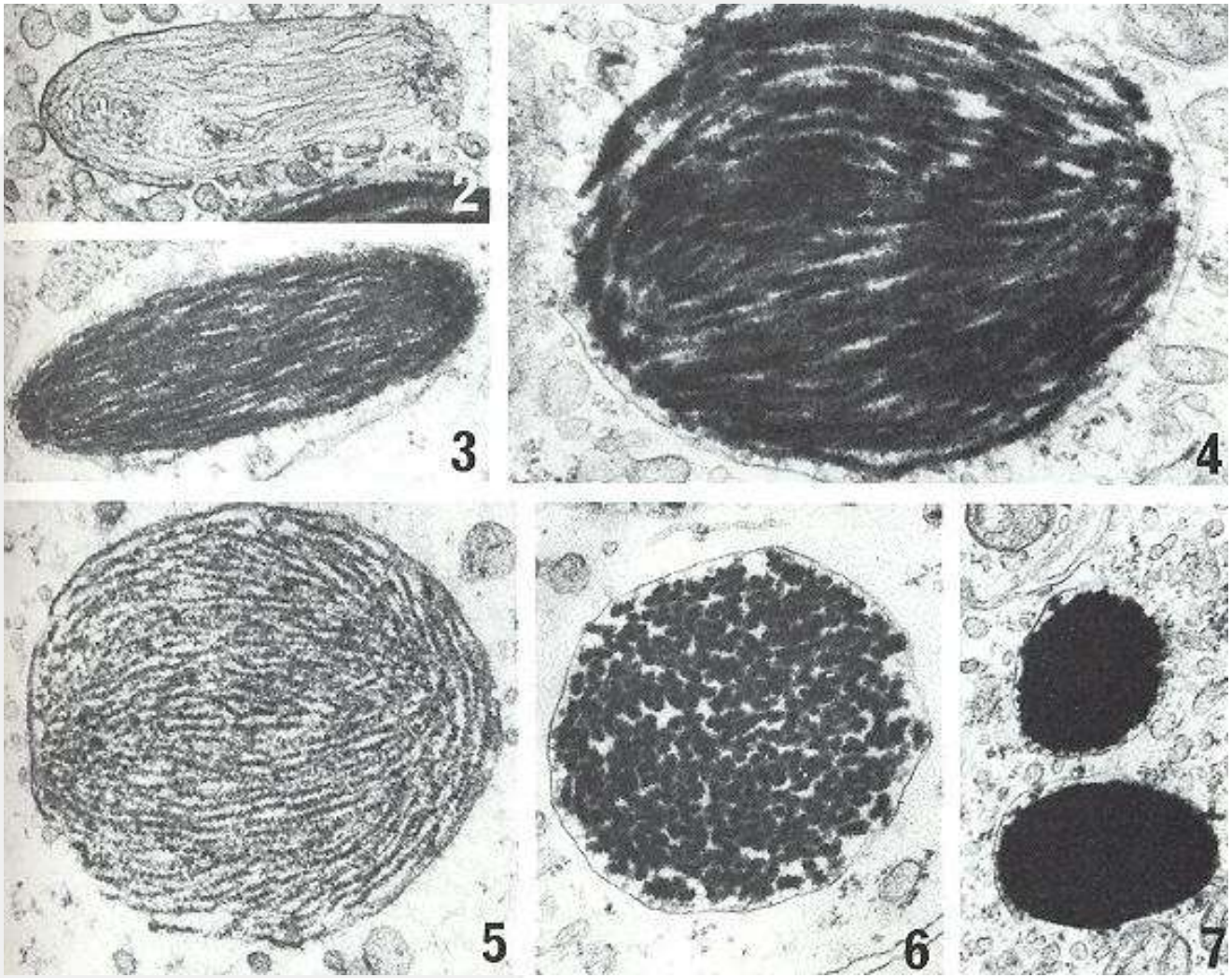




Amelanotic melanoma

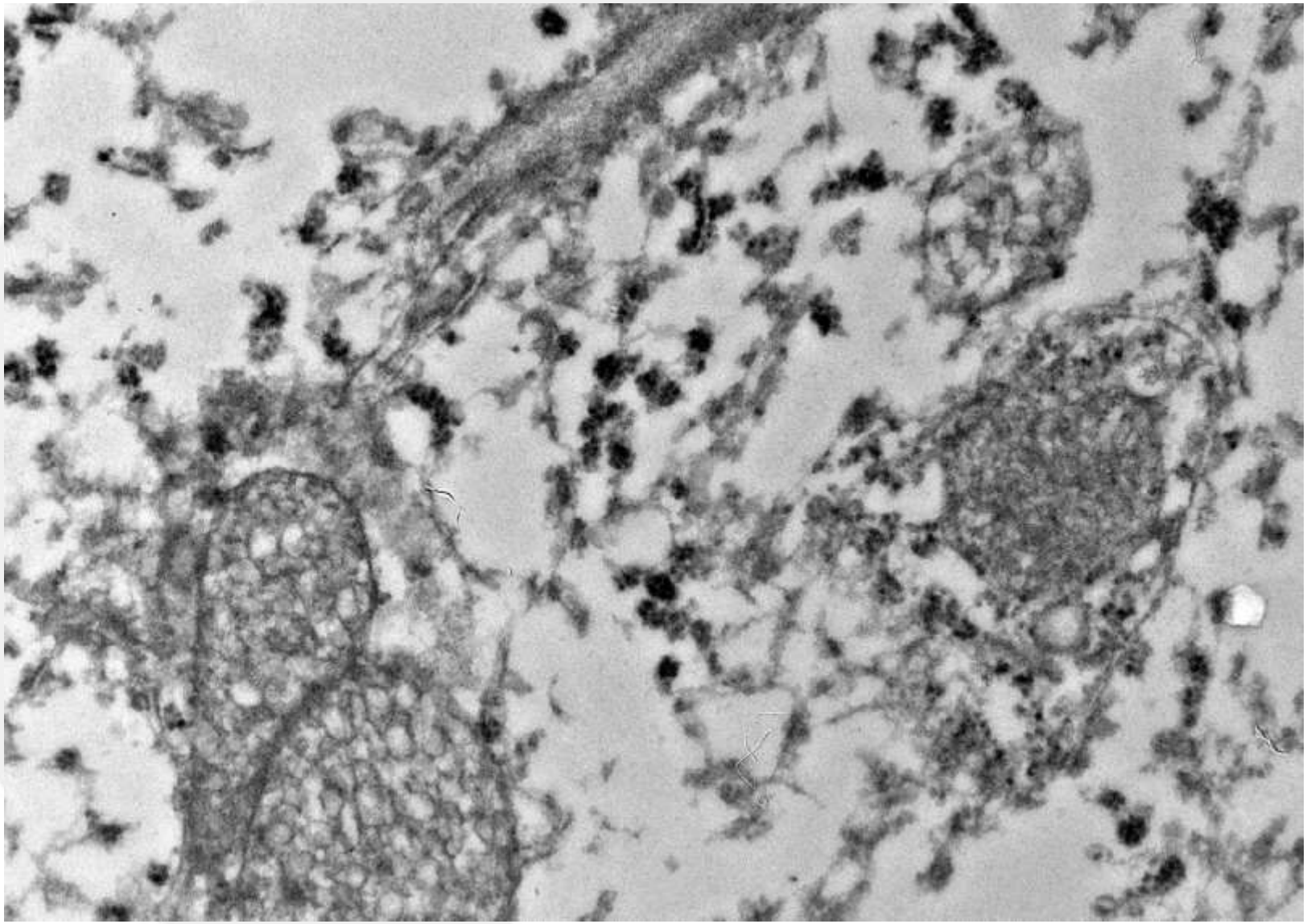


Amelanotic melanoma: Ultrastructure

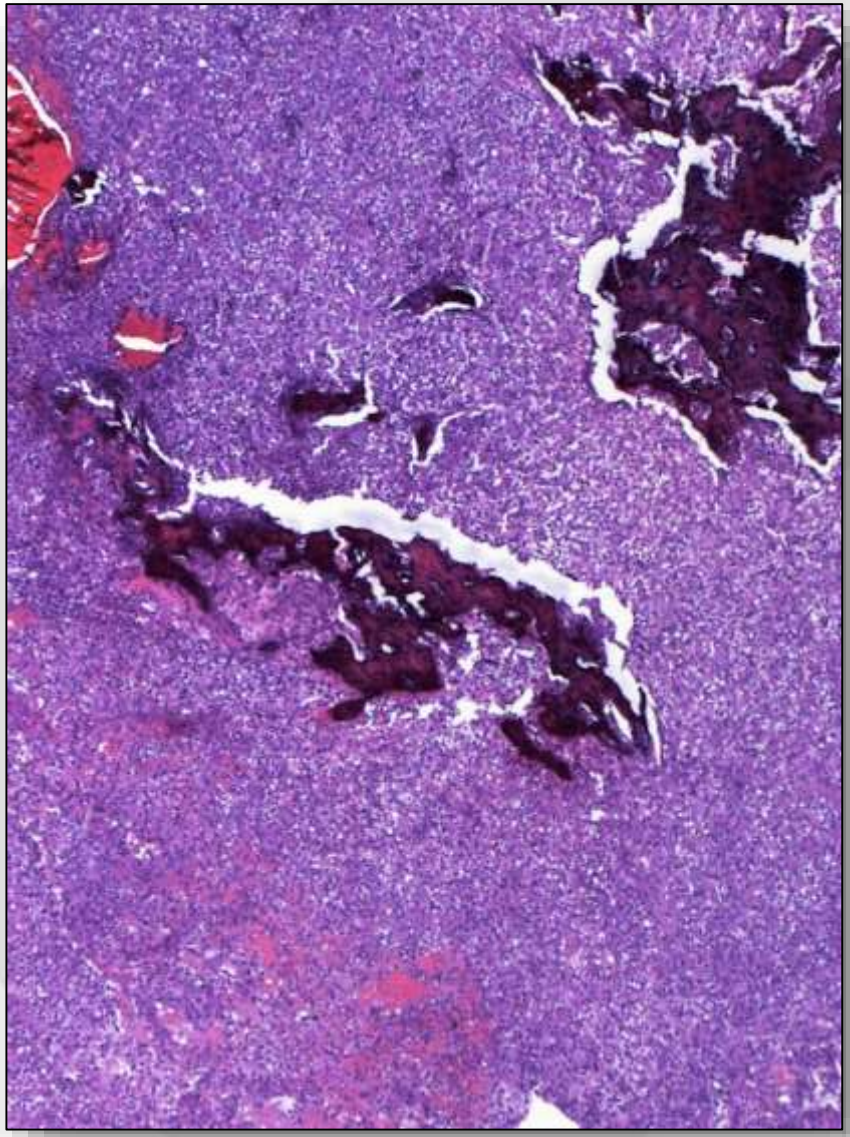


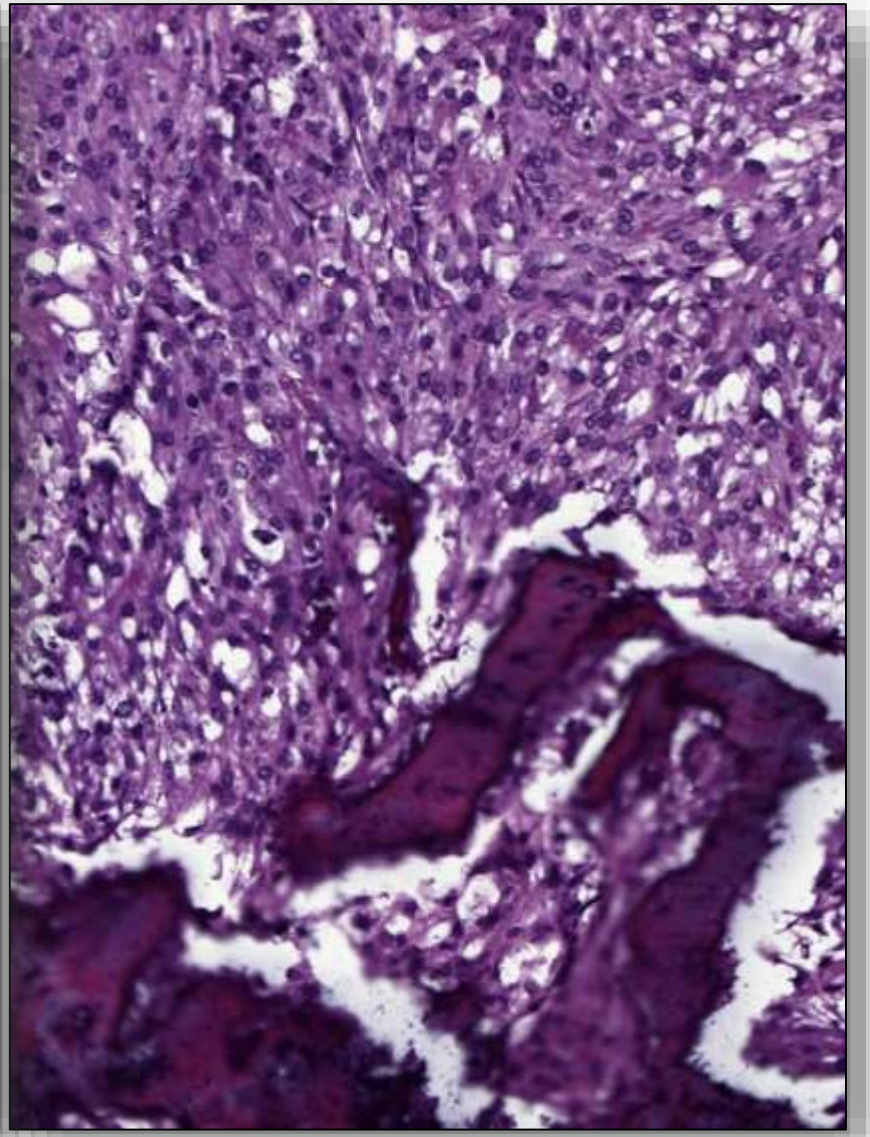
2. Stage II (premelanosome), 3-6. Stage III, 7. Stage IV (Ghadially 1982)

Amelanotic melanoma: Ultrastructure

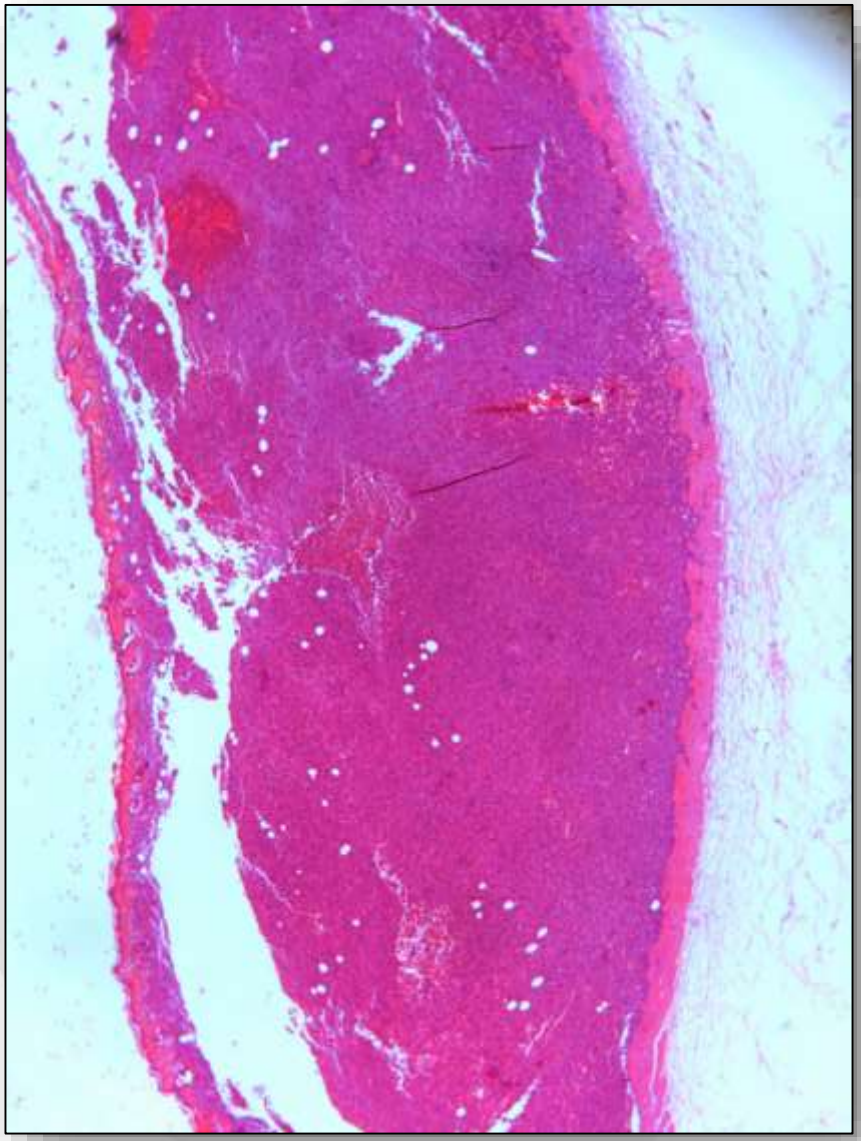


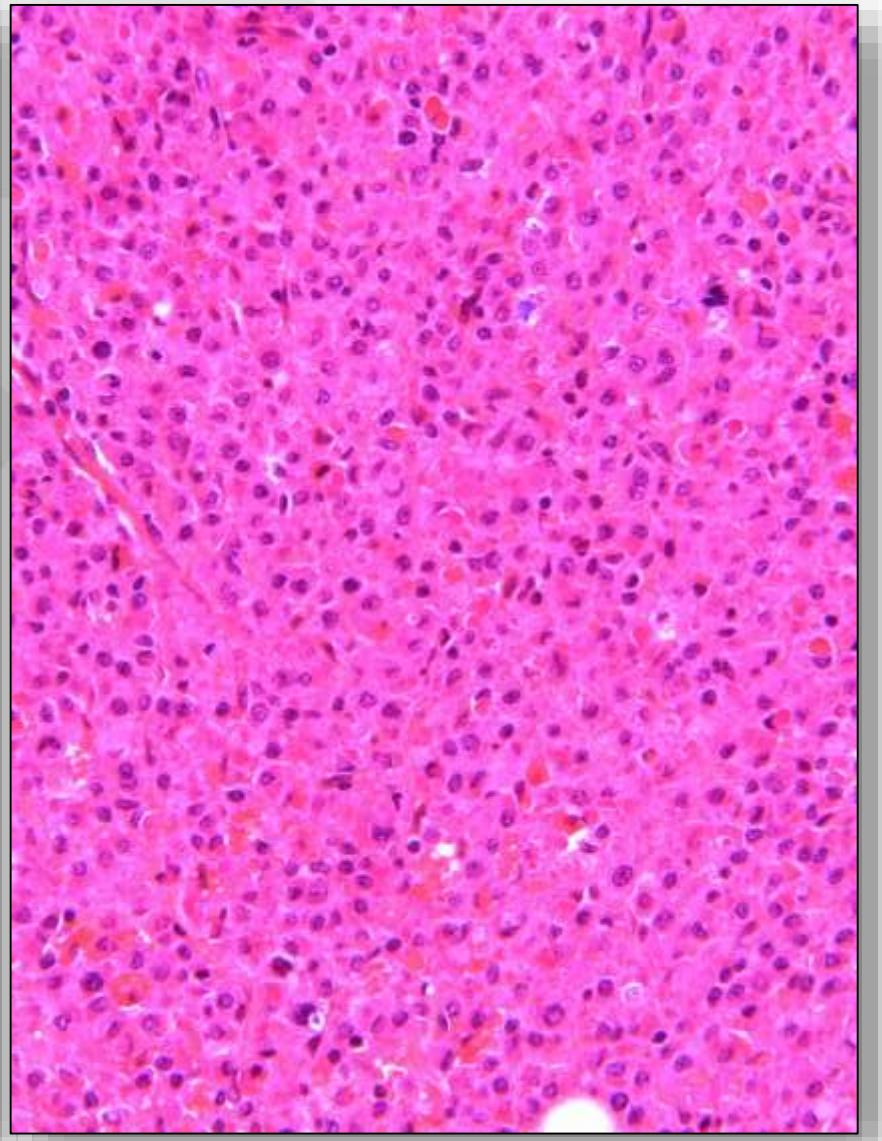
Oestosarcoma (CD-1 mice)



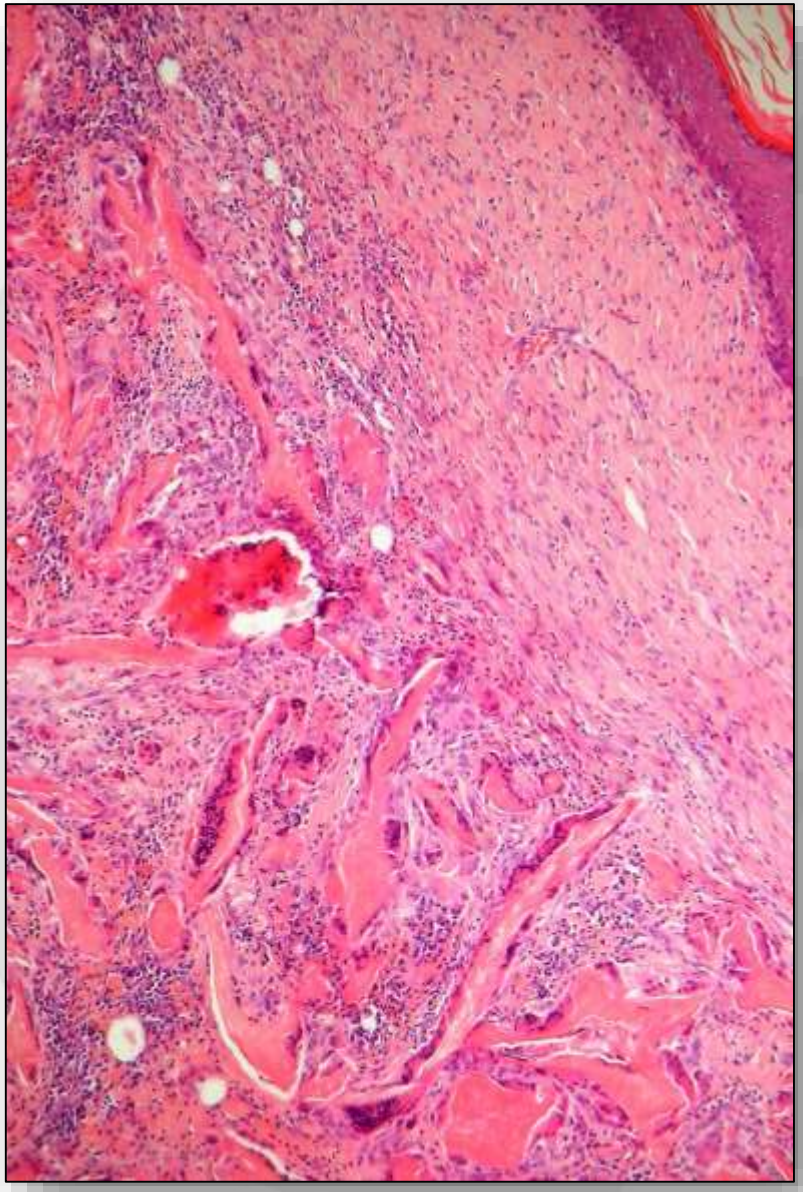


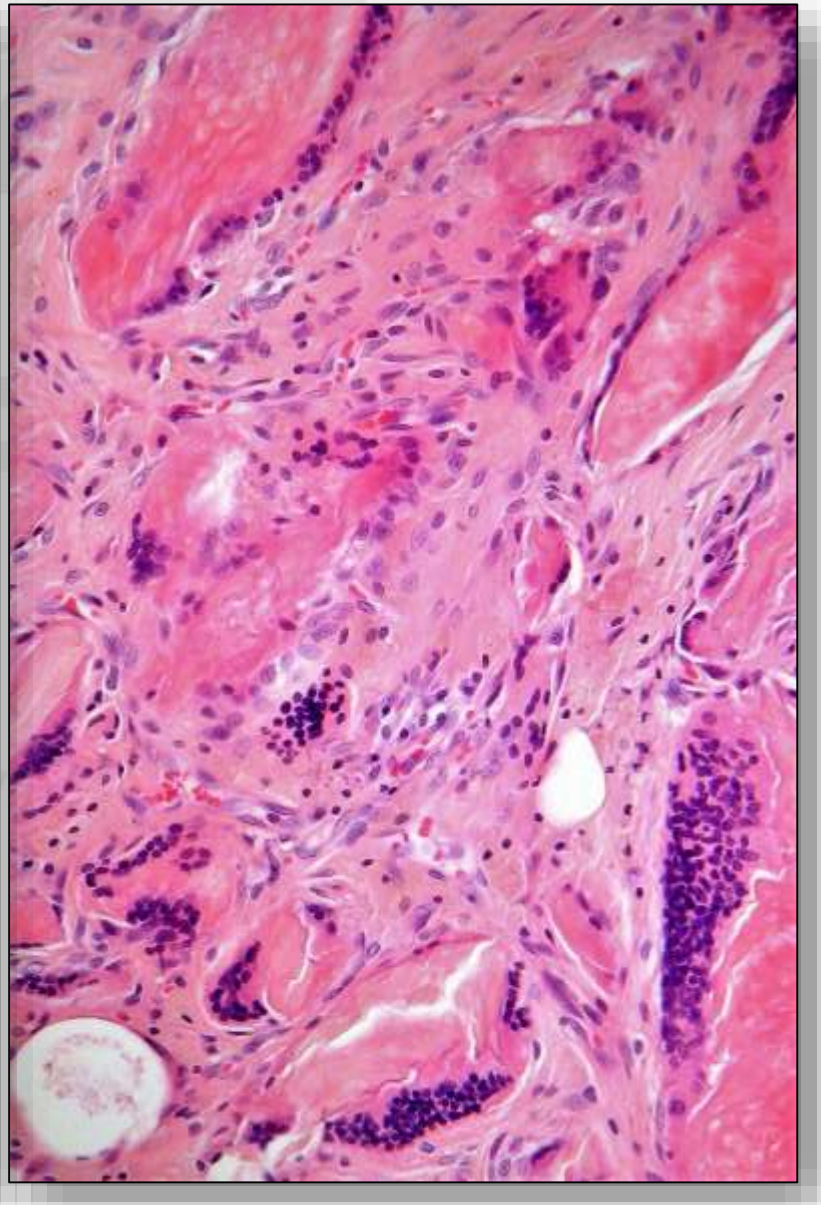
Mast cell tumor: B57BL/6 mouse



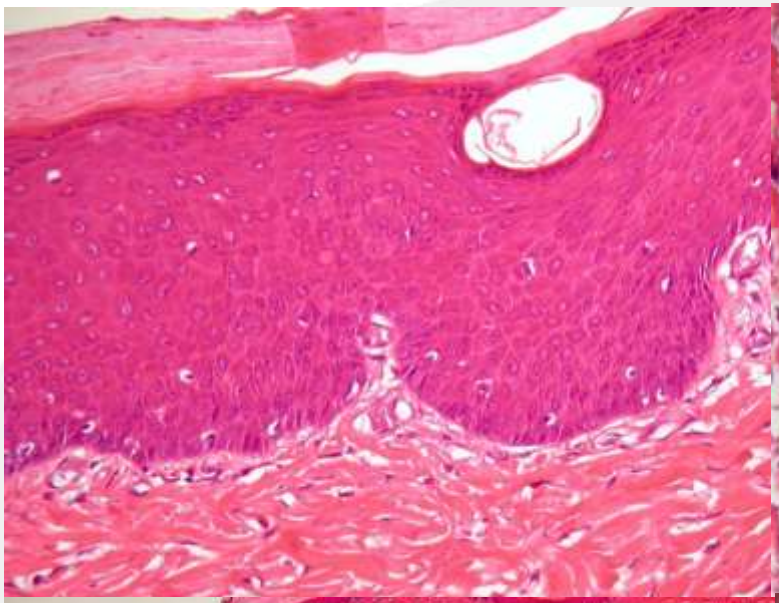


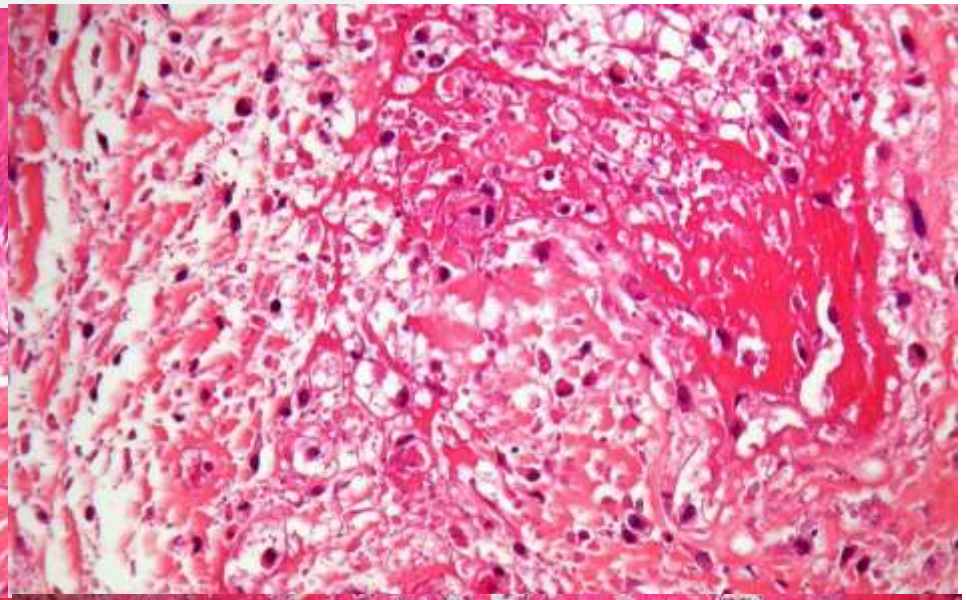
Rat: Syringoma?

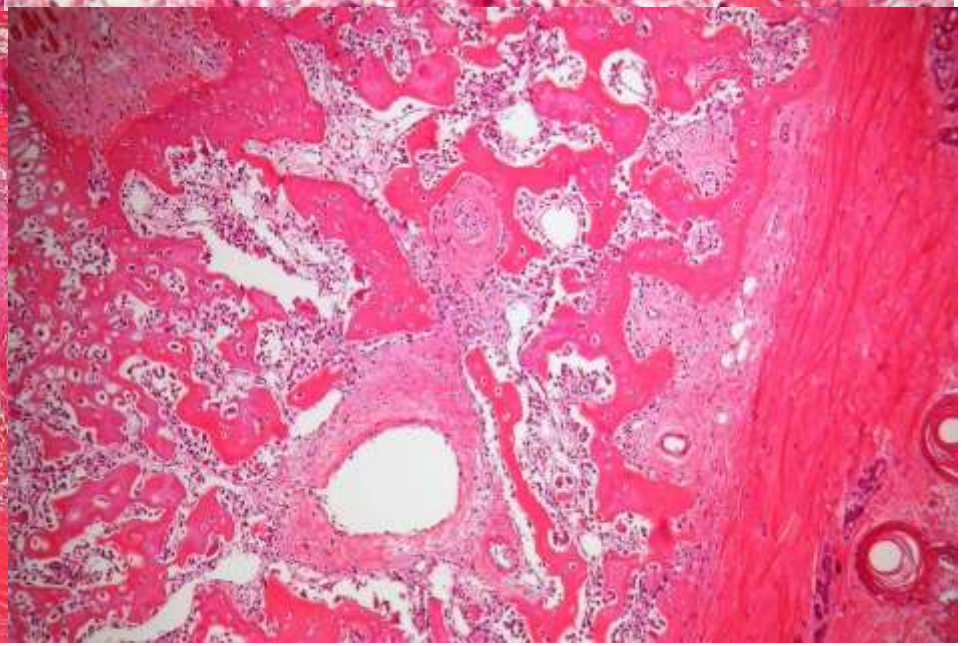




Findings on Tail

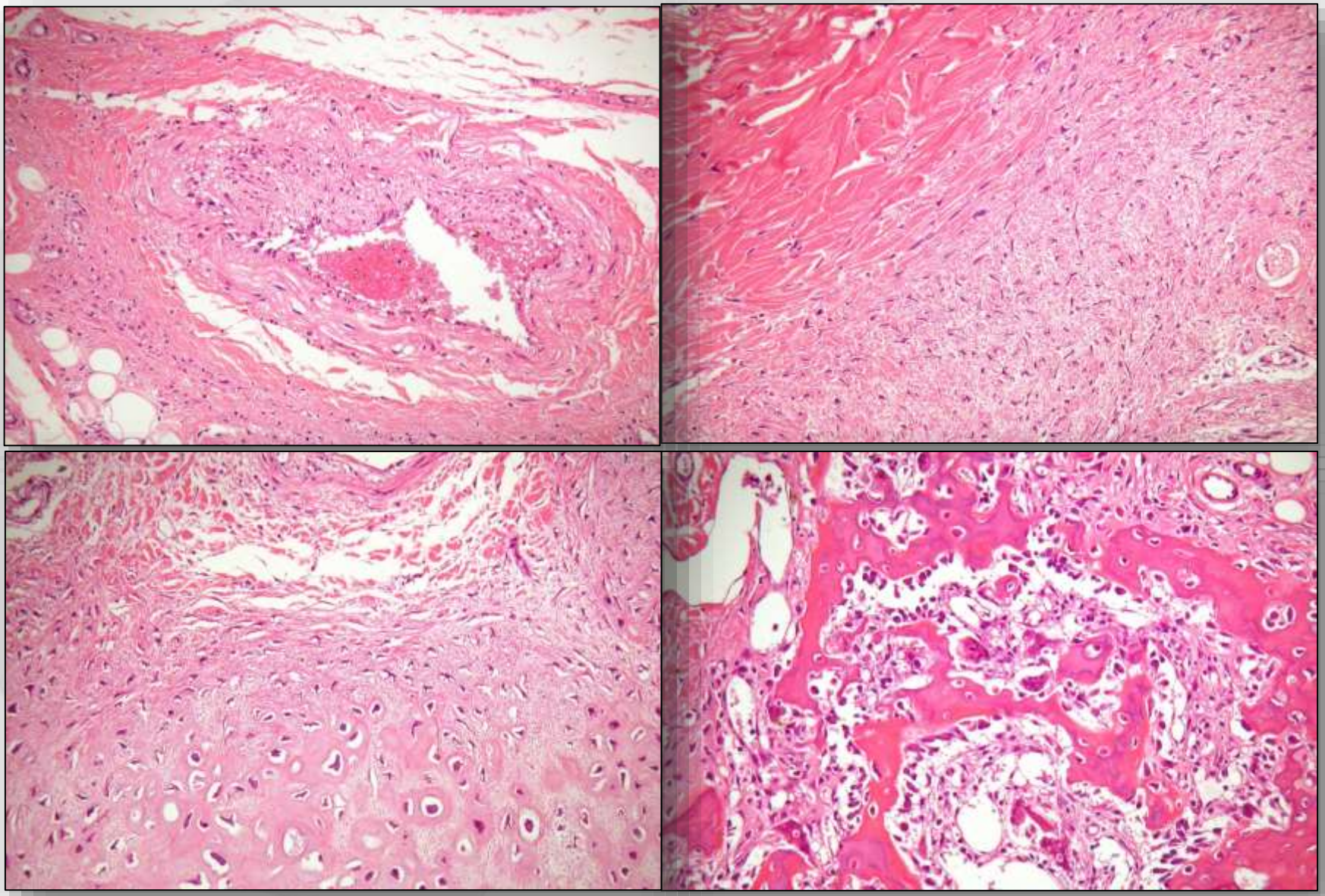




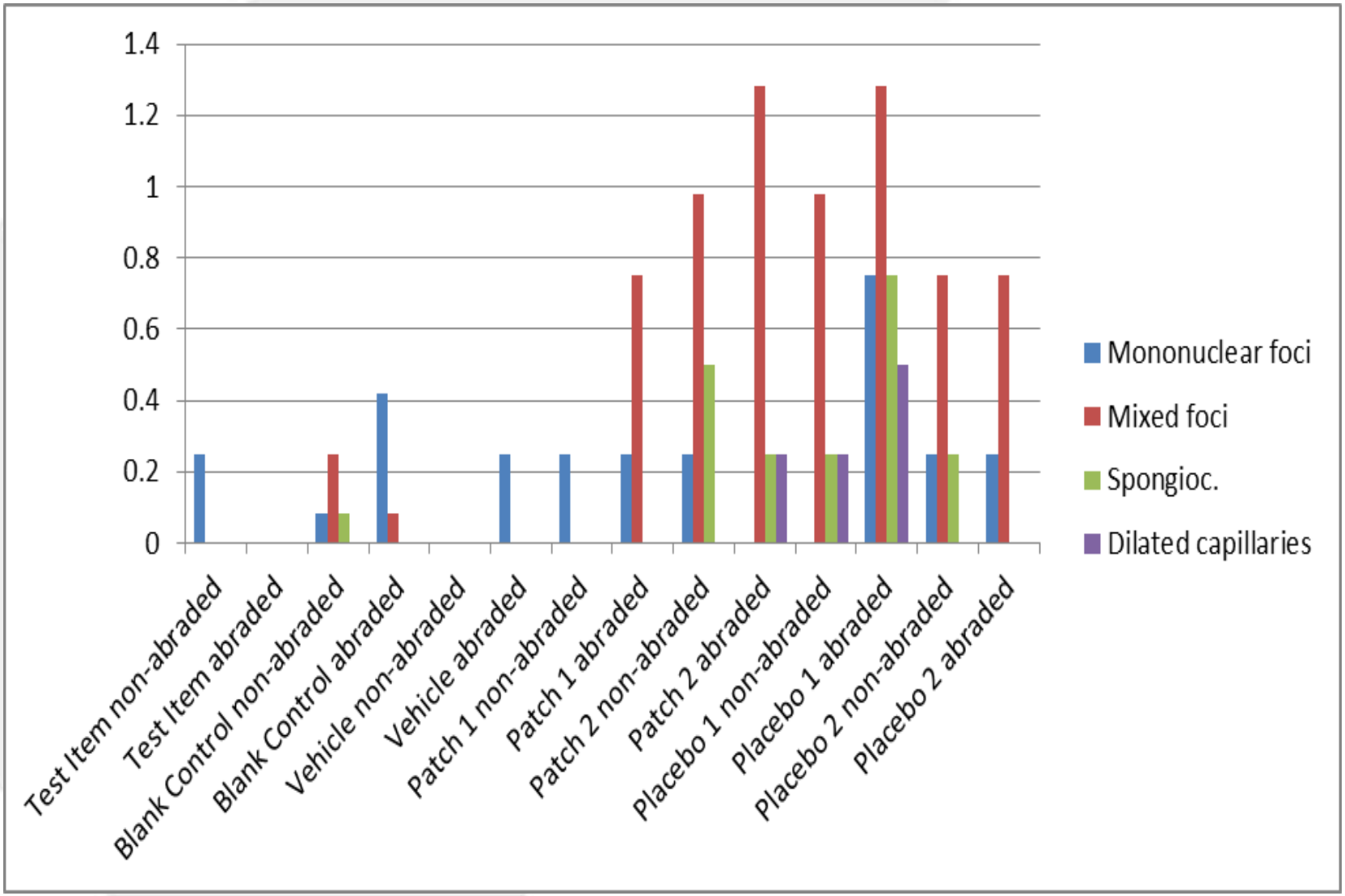


Findings on Tail: Induced (hGF

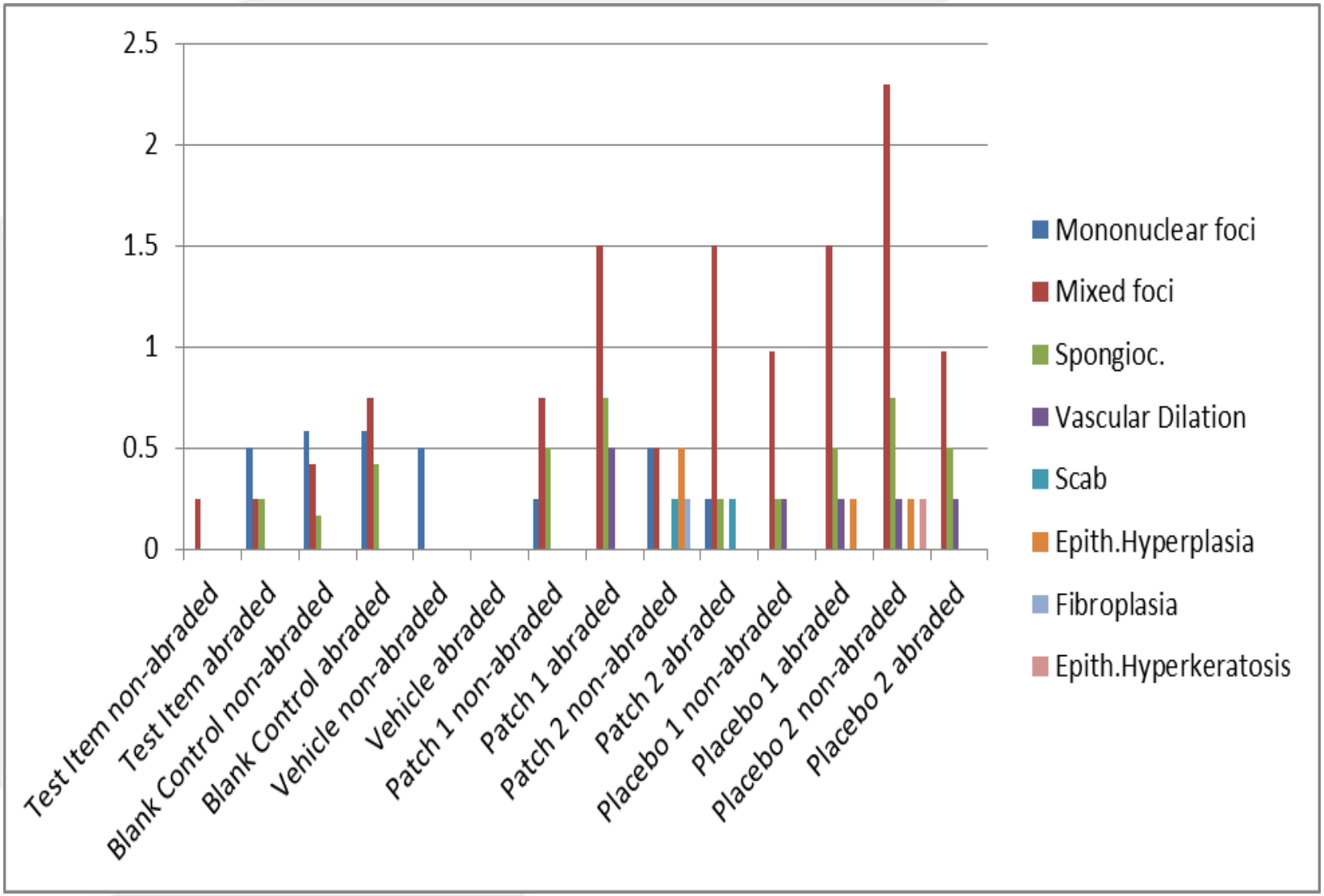
phlebitis (1), fibrosis (2), chondrous metaplasia (3), osseous metaplasia (4)



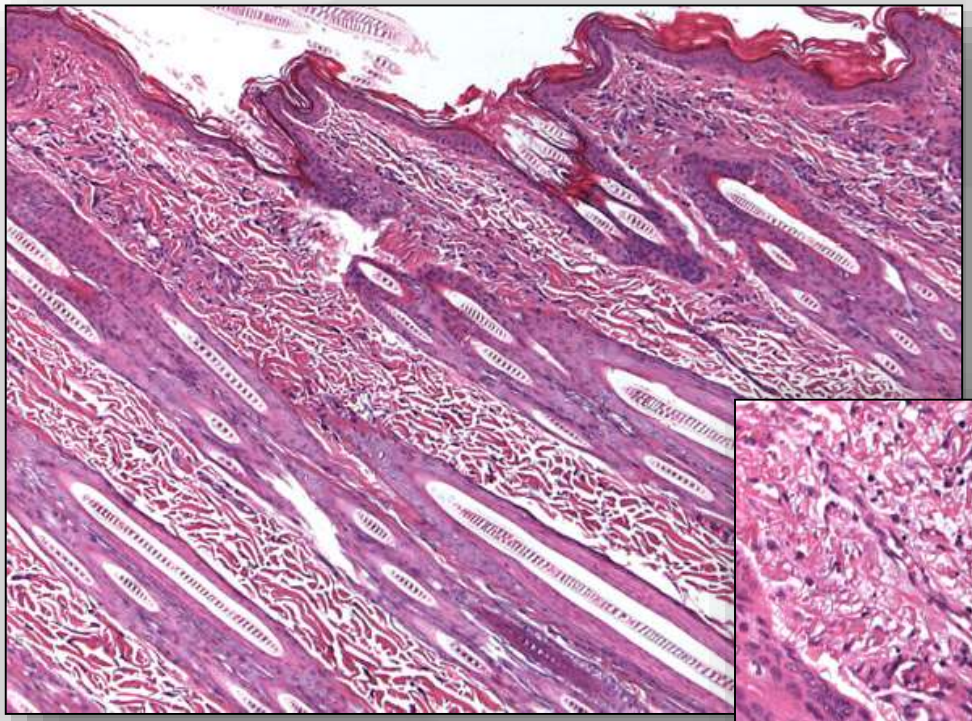
Rabbit: Example, Males



Rabbit: Example, Females

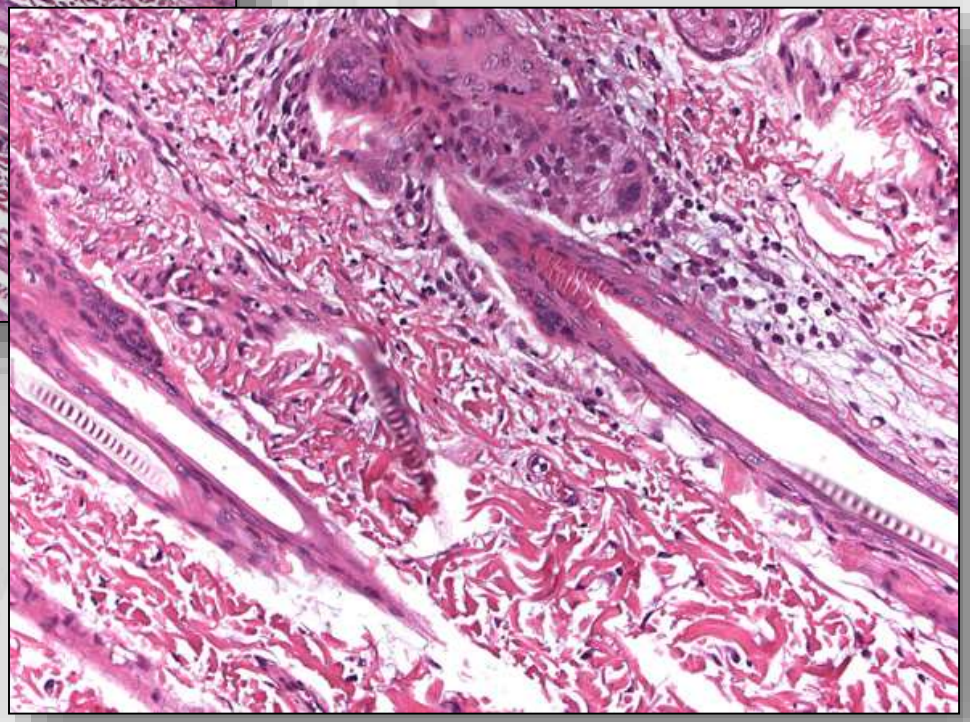


Rabbit: Examples, Non-Abraded, Control

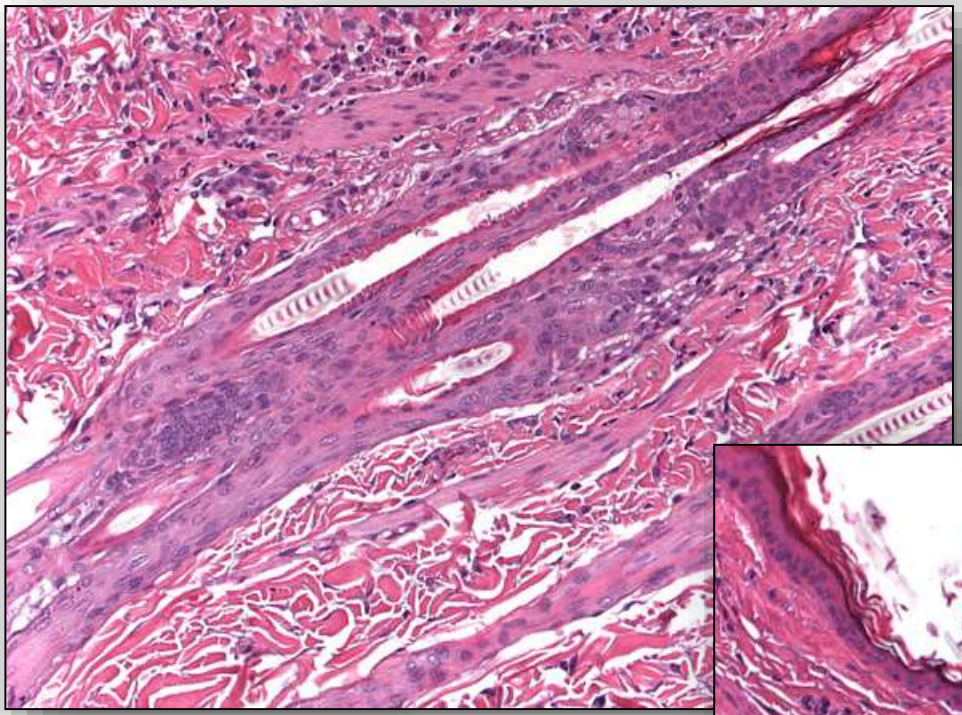


Mononuclear cell foci

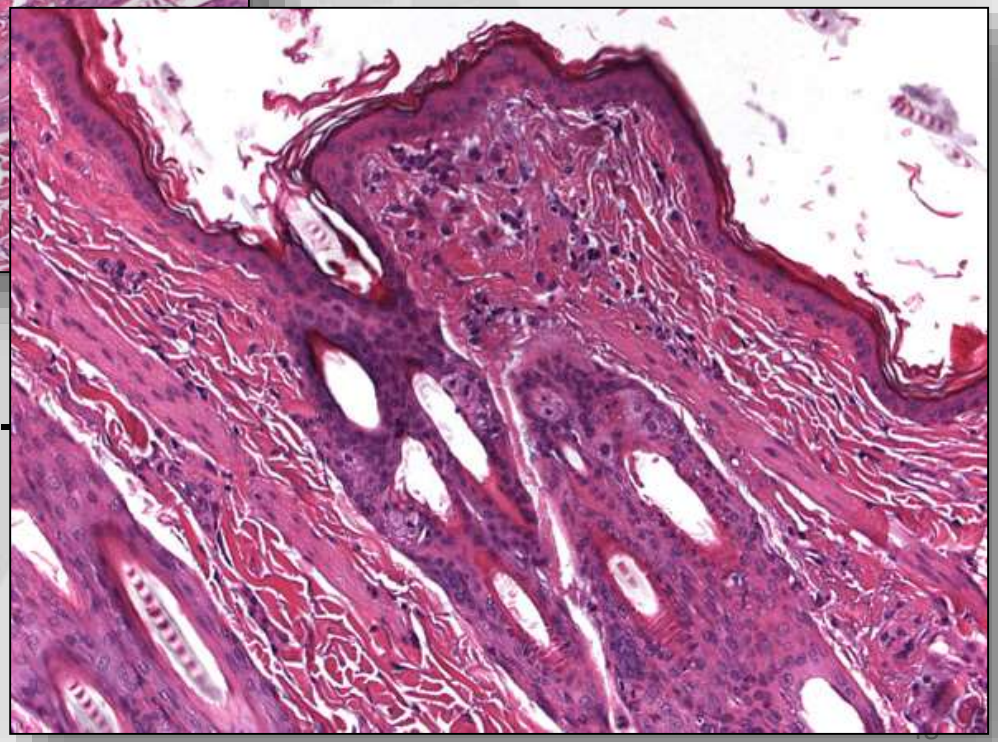
Mixed inflammatory cells



Rabbit: Examples, Abraded, Control

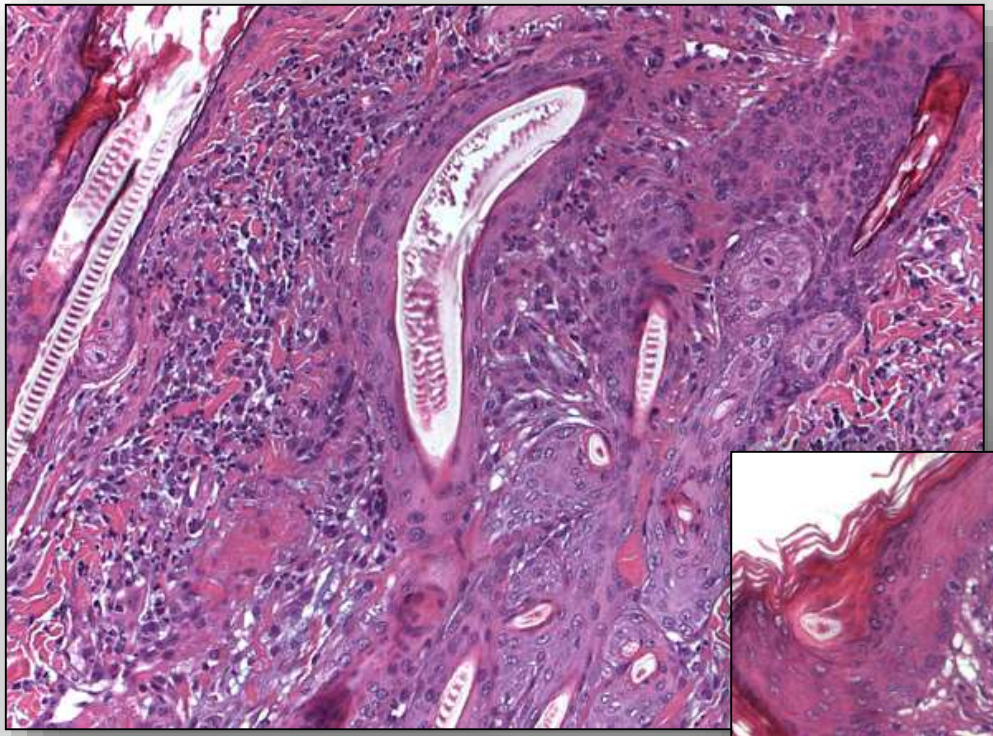


Mononuclear cell foci

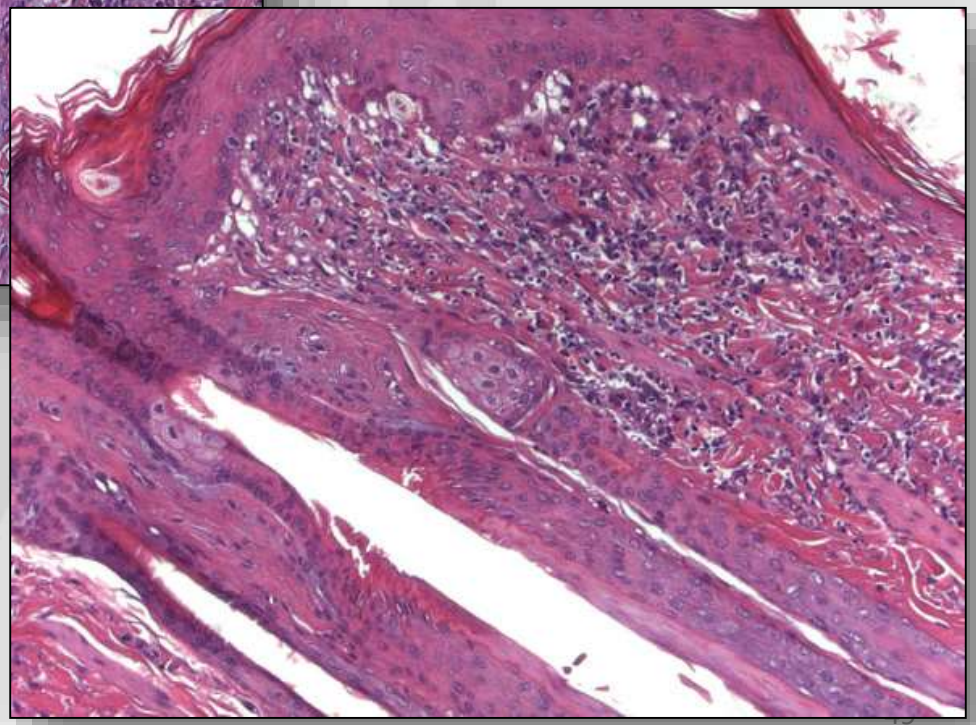


Spongiotic subepidermal muscle fibers and epithet-lia and mixed inflamma-tory cells

Rabbit: Examples, Abraded, Control



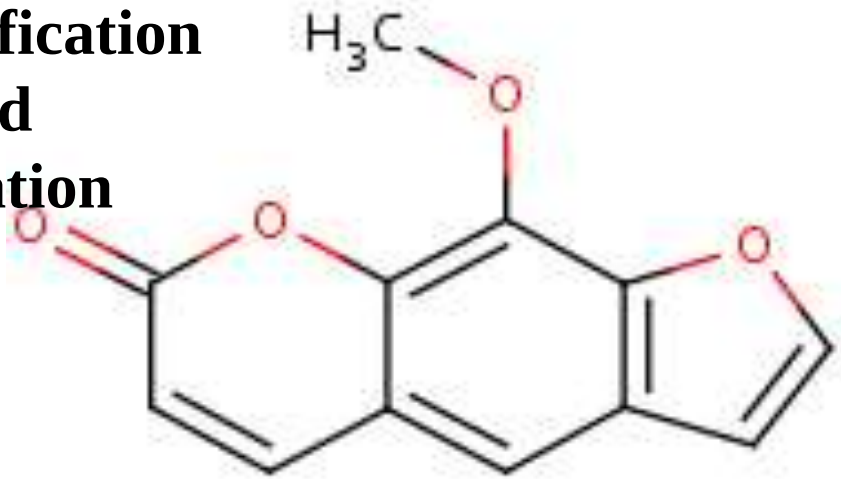
Spongiotic subepidermal muscle fibers and epithet-lia and mixed inflamma-tory cells (non-abraded)



Spongiotic subepidermal muscle fibers and epithet-lia and mixed inflamma-tory cells (abraded)

8-Methoxypsoralen (8-MOP)

- **Cumarin derivate**
- **Treatment of skin diseases, i.e. psoriasis vulgaris, cutaneous T-cell lymphomas (e.g. Mycosis fungoides), vitiligio**
- **Skin pigmentizer**
- **Applied in combination with a radiation therapy UV)**
- **e.g.Uvadex® and Meladinine®.**
- **Induction of cell membrane damage, DNA crosslinking and binding to a cytosolic proteins that finally cause apoptosis, modification of membrane antigenicity and antigen presenting cell activation immunosuppressive (mechanism not established)**



Materials and Methods - Study Design

- **Female HsdBlu:LE (SPF) Long Evans rats**
- **Age: 8 – 10 weeks**
- **Body weight: 177g – 209 g**

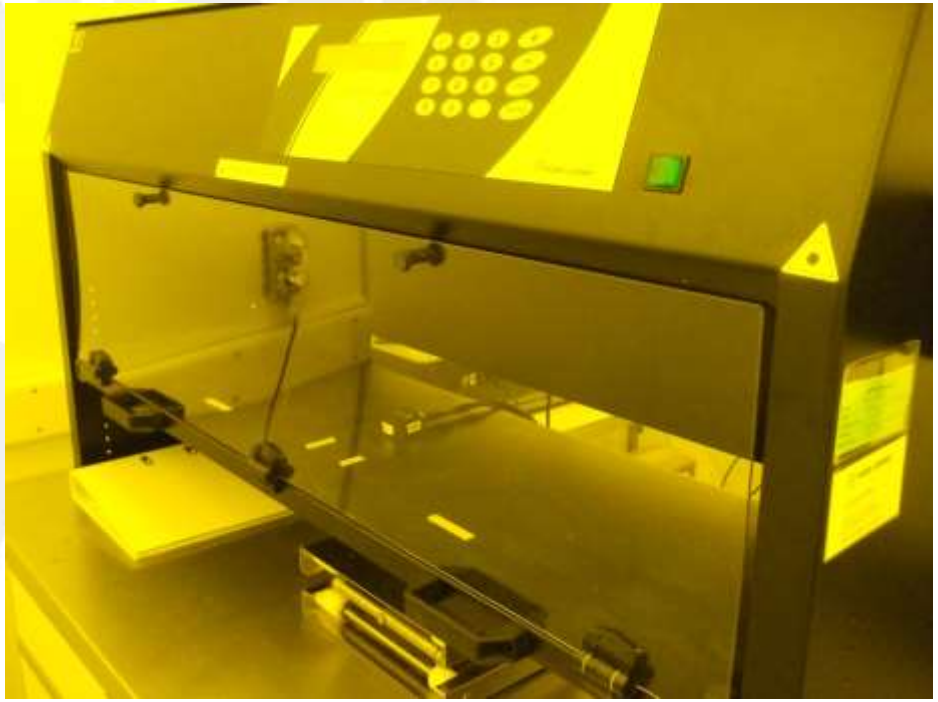
Allocation and Dose Levels mg/kg bw	Group 1 Control 0	Group 2 5.0
Females	1 - 6	7 - 12

Treatment and related procedures

- **Pigmented and unpigmented skin sites on left flank shaved 24 h before 8-MOP application**
- **Single oral (gavage) dose of 5 mg/kg at a dose volume of 5 ml/kg**
- **Anesthetized (33 mg/kg pentobarbitone i.p.) approximately 30 min after 8-MOP application for irradiation**
- **Laid on right flank and covered with aluminum foil (including feet) with holes at the irradiation sites during the irradiation procedure**
- **irradiated left eye moistened every 10 min /0.9% NaCl)**
- **contralateral eye protected with ophthalmic cream (vitamin A <blanche>; Bausch & Lomb Swiss AG)**

UV-A Irradiation

- **UV-A irradiation approximately 1 h after 8-MOP application in a Bio-Spectra irradiation chamber (Vilber Lourmat Deutschland GmbH)**
- **UV-A source 3 x T-40.L UV-A tubes / 365 nm / 40 Watt**
- **Peak wave length 365 nm**
- **Intensity max. 4.01 mW/cm^2**
- **Radiation dose 35 J/cm^2 UV-A**



In-Live: Skin

	Assessment of Skin Reactions (hours after completion of UV-A irradiation)			
	(4 hours)	(20 hours)	(24 hours)	(48 hours)
	Pigmented Skin			
Group 1 Vehicle Control	Grade 0: 0 Grade 1: 6 Grade 2: 0 Grade 3: 0	Grade 0: 0 Grade 1: 5 Grade 2: 1 Grade 3: 0	Grade 0: 0 Grade 1: 6 Grade 2: 0 Grade 3: 0	Grade 0: 1 Grade 1: 5 Grade 2: 0 Grade 3: 0
Group 2 5.0 mg/kg bw 8-Methoxypsoralen	Grade 0: 0 Grade 1: 4 Grade 2: 2 Grade 3: 0	Grade 0: 0 Grade 1: 4 Grade 2: 2 Grade 3: 0	Grade 0: 0 Grade 1: 0 Grade 2: 4 Grade 3: 2	Grade 0: 0 Grade 1: 0 Grade 2: 4 Grade 3: 2
	Unpigmented Skin			
Group 1 Vehicle Control	Grade 0: 0 Grade 1: 6 Grade 2: 0 Grade 3: 0	Grade 0: 0 Grade 1: 5 Grade 2: 1 Grade 3: 0	Grade 0: 0 Grade 1: 2 Grade 2: 4 Grade 3: 0	Grade 0: 0 Grade 1: 2 Grade 2: 4 Grade 3: 0
Group 2 5.0 mg/kg bw 8-Methoxypsoralen	Grade 0: 0 Grade 1: 6 Grade 2: 0 Grade 3: 0	Grade 0: 0 Grade 1: 6 Grade 2: 0 Grade 3: 0	Grade 0: 0 Grade 1: 0 Grade 2: 6 Grade 3: 0	Grade 0: 0 Grade 1: 0 Grade 2: 6 Grade 3: 0

N°	Assessment of Skin Reactions (hours after completion of UV-A irradiation)							
Group 1 – Vehicle Control								
	(4 hours)*		(20 hours)*		(24 hours)		(48 hours)	
	Pigm. skin	Unpigm skin	Pigm. skin	Unpigm skin	Pigm. skin	Unpigm skin	Pigm. skin	Unpigm skin
1	1	1	1	1	1	2	1	2
2	1	1	1	2	1	2	0	2
3	1	1	2	1	1	2	1	2
4	1	1	1	1	1	1	1	1
5	1	1	1	1	1	1	1	1
6	1	1	1	1	1	2	1	2
Group 2 – 5.0 mg/kg bw 8-Methoxypsoralen								
	(4 hours)*		(20 hours)*		(24 hours)		(48 hours)	
	Pigm. skin	Unpigm skin	Pigm. skin	Unpigm skin	Pigm. skin	Unpigm skin	Pigm. skin	Unpigm skin
7	1	1	1	1	2	2	2	2
8	2	1	2	1	3	2	3	2
9	1	1	1	1	2	2	2	2
10	1	1	1	1	2	2	2	2
11	2	1	2	1	3	2	3	2
12	1	1	1	1	2	2	2	2

Demo, Evans-blue dye leakage after 24 hours

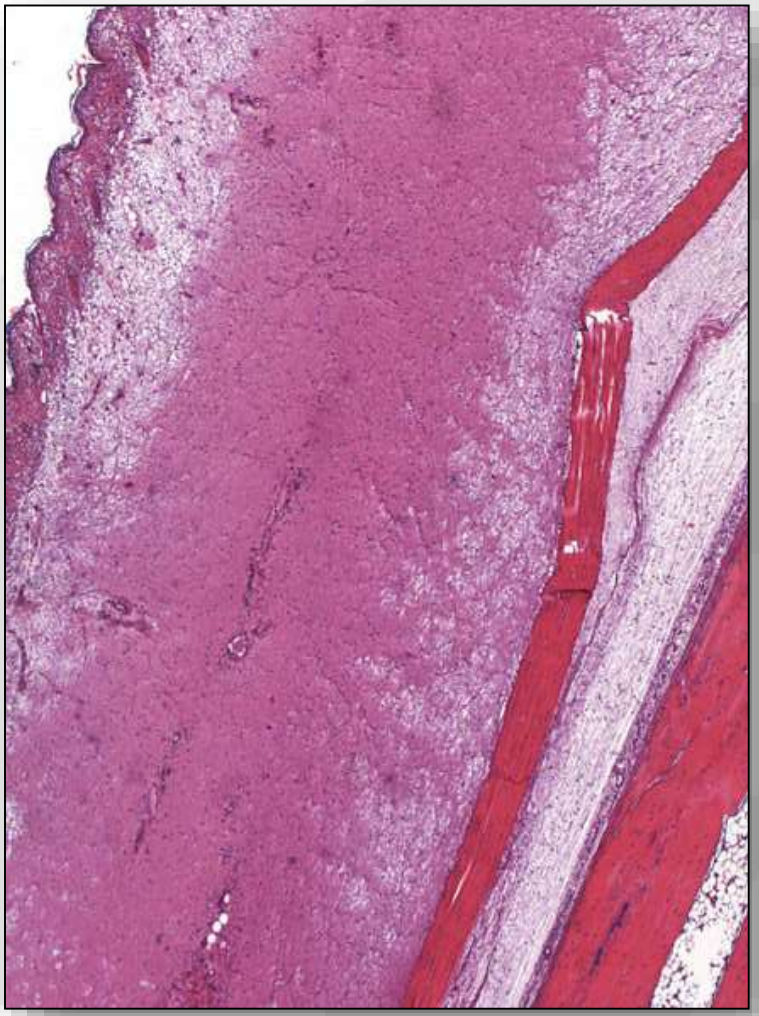
Demo, Evans-blue dye leakage after 48 hours

Necropsy/histology

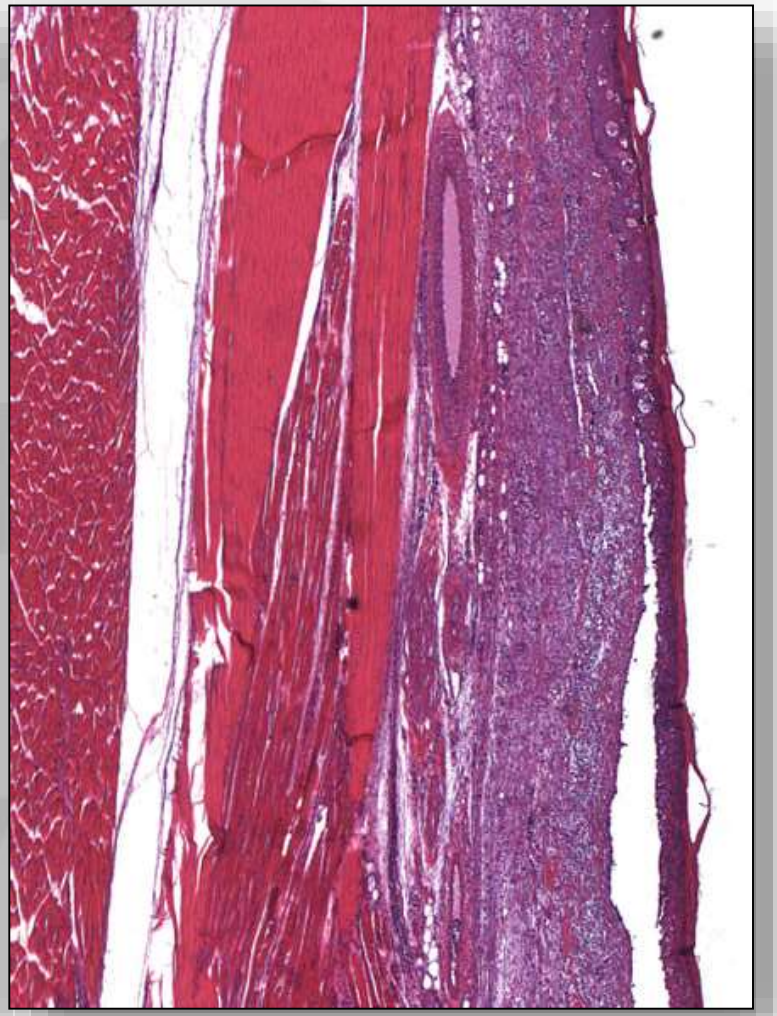
- **Swollen Hind feet in all 8-MOP-treated animals**
- **No further gross lesions**

Finding / Groups	1	2
Total Affected / Mean Severity	(6) F	(6) F
Epidermal necrosis	0	6/2.5
Spongiosis, subepidermal	0	5/1.8
Spongiosis, epidermal	0	4/1.8
Dermal edema	0	6/4.0
Pododermatitis	0	6/3.3

Histopathology: Feet

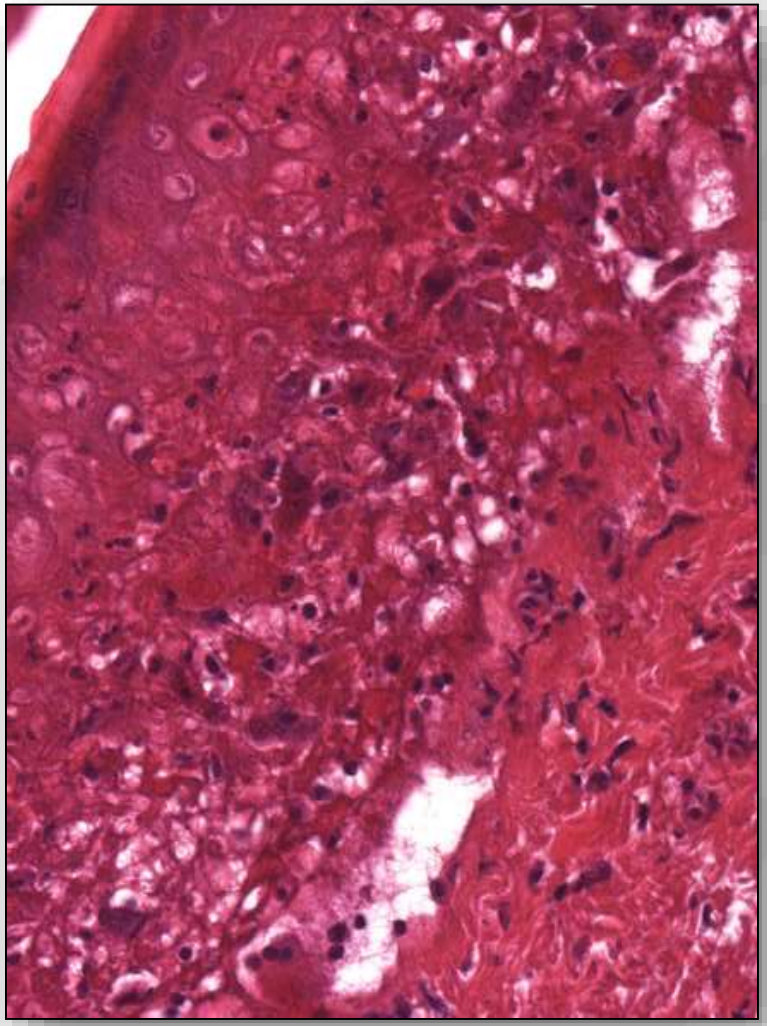


Foot: Marked dermal edema

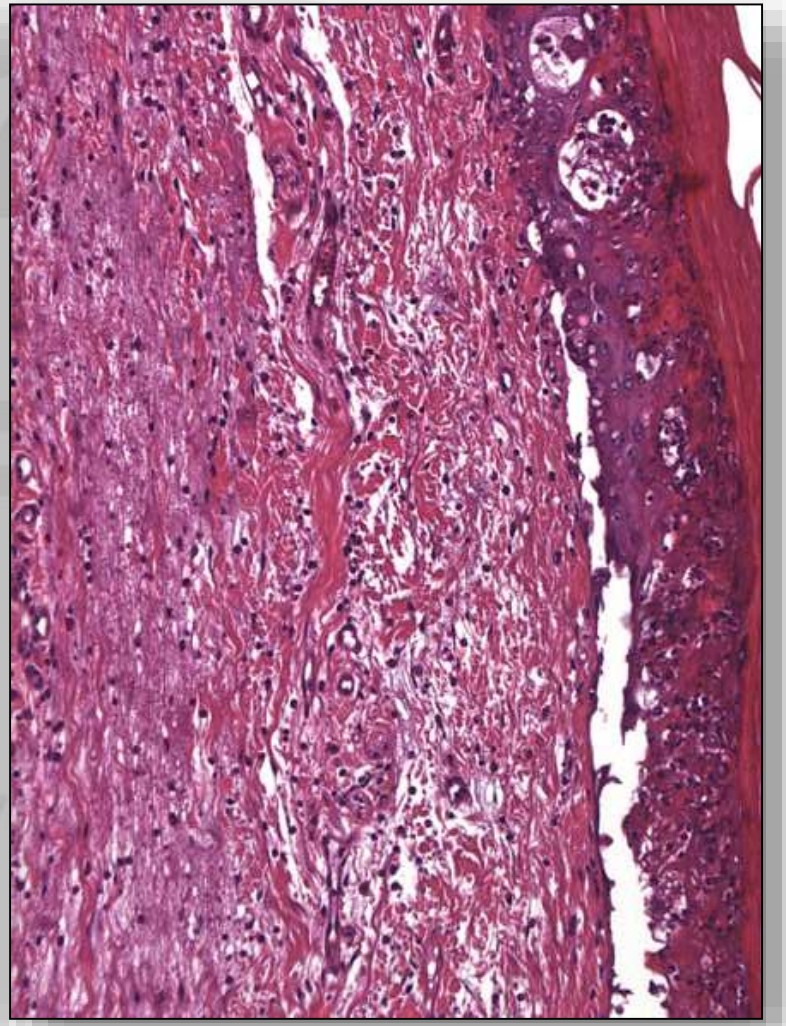


Foot: Pododermatitis with epidermal necrosis characterized by laceration

Histopathology: Feet



Acute to subacute pododermatitis (necrotizing).

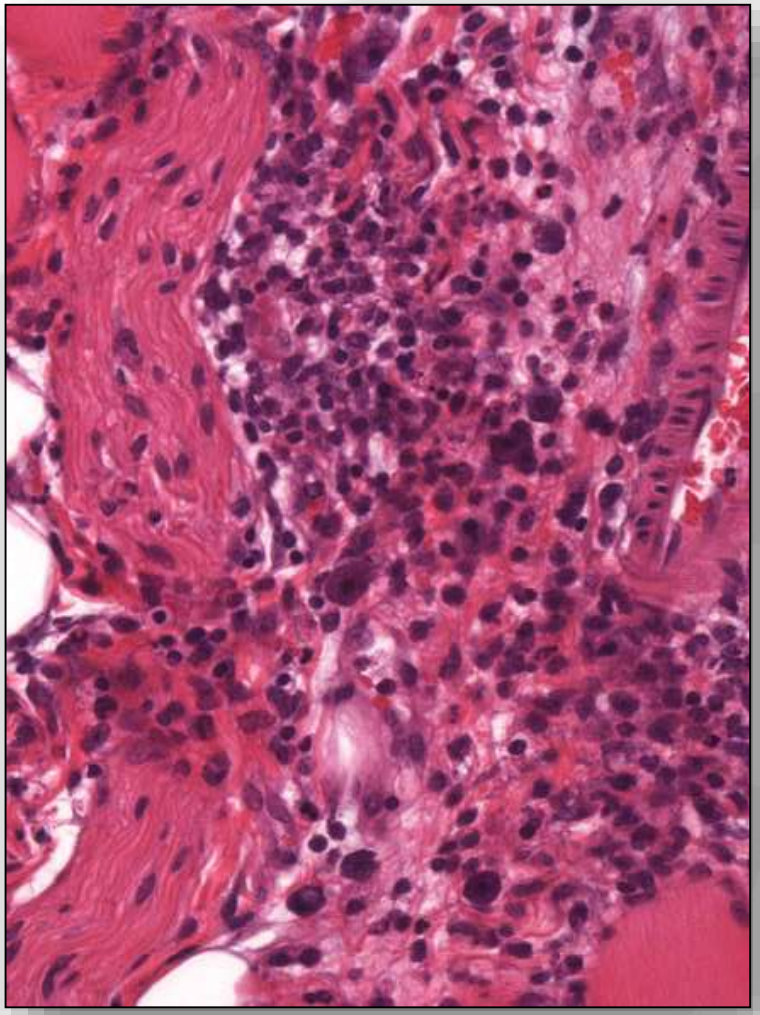


Pododermatitis with epidermal necrosis. Note laceration and epidermal spongiosis

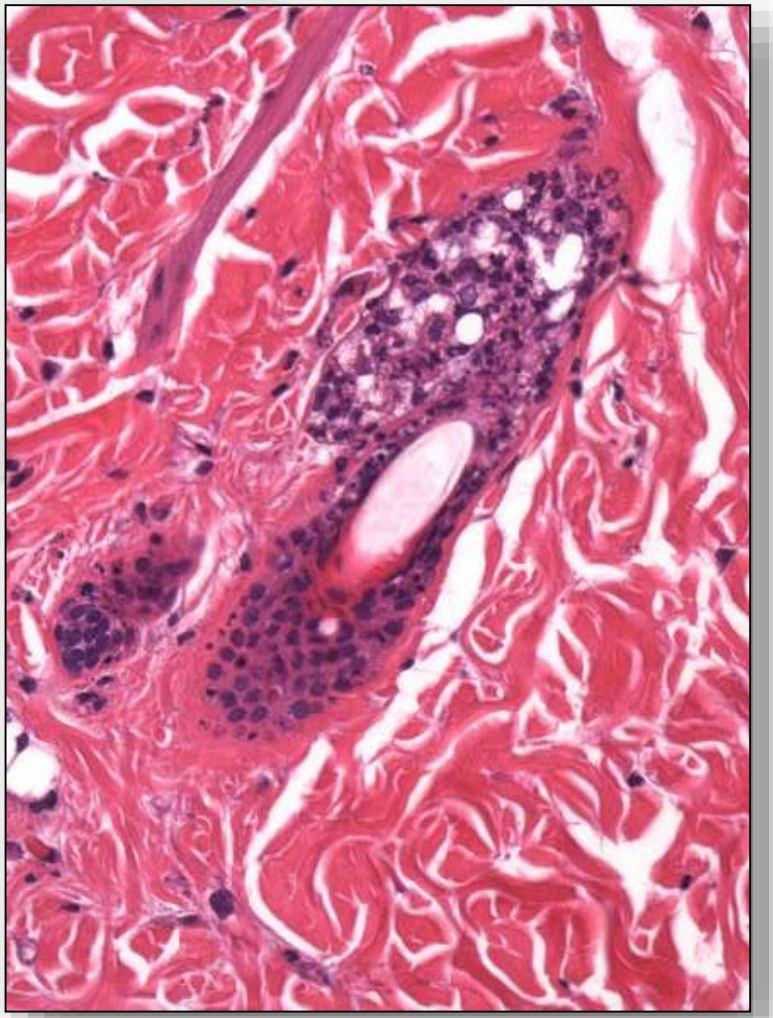
Histopathology: Non-pigmented skin

Finding / Groups	1	2	Finding / Groups	1	2
Pigmented Skin					
Unirradiated			Irradiated		
Total Affected / Mean Severity	(6) F	(6) F	Total Affected / Mean Severity	(6) F	(6) F
Hyperkeratosis	0	0	Hyperkeratosis	1/1.0	0
Epidermal hyperplasia	1/1.0	0	Epidermal hyperplasia	2/1.5	5/2.4
Focal erosion/scab	1/1.0	0	Focal erosion/scab	2/1.0	4/1.8
Ulceration	0	0	Ulceration	0	5/2.6
Follicular inflammation	0	0	Follicular inflammation	0	5/1.2
Subcutaneous infiltration	0	0	Subcutaneous infiltration	1/1.0	0
Epidermal necrosis	0	0	Epidermal necrosis	0	6/3.8
Dermal inflammation	0	0	Dermal inflammation	0	6/2.7
Subcutaneous inflammation	0	0	Subcutaneous inflammation	0	6/1.8

Histopathology: Non-pigmented skin

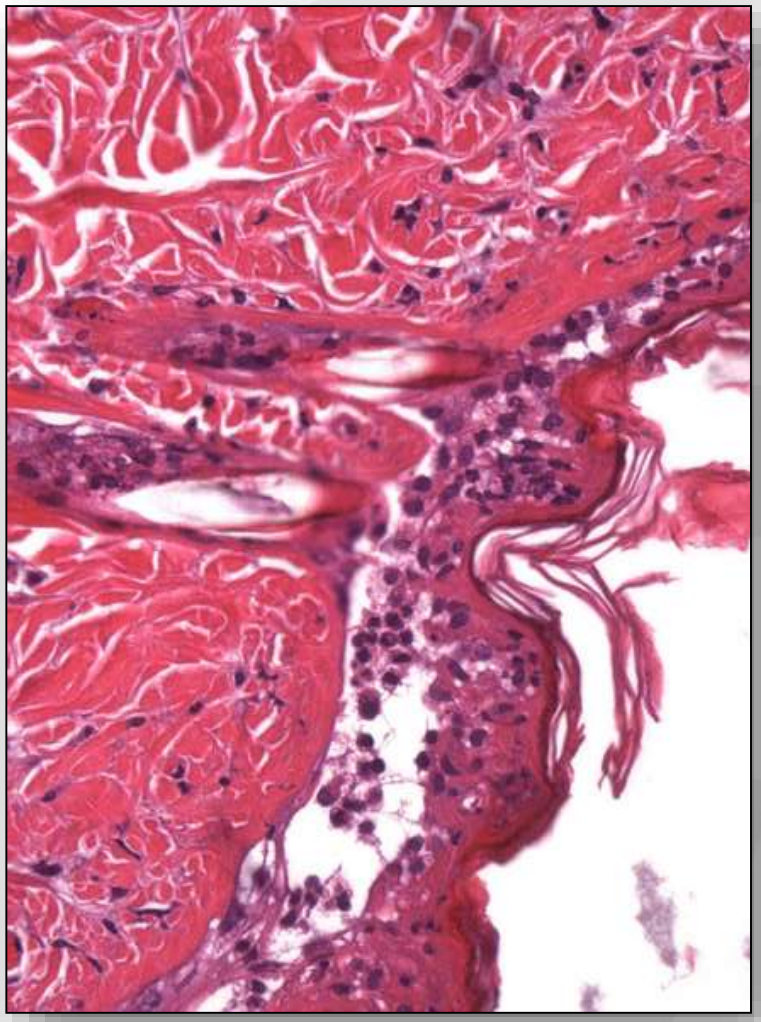


Dermatitis, mainly mono-nuclear and plasma cells

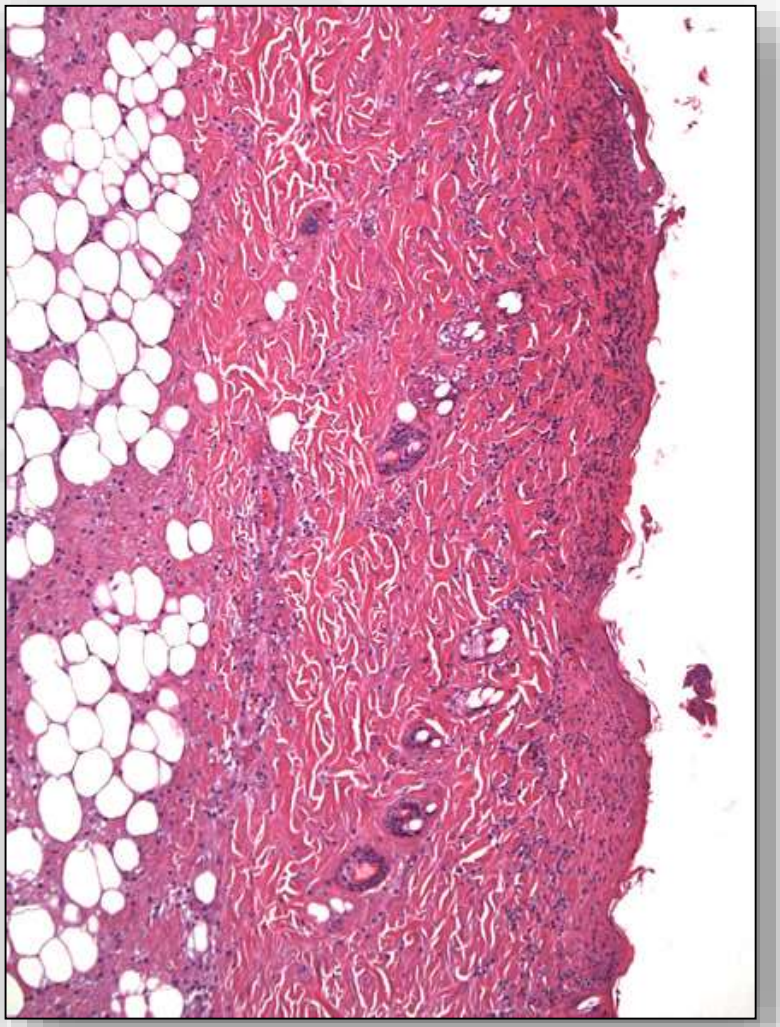


Folliculitis characterized by necrotic sebaceous glands

Histopathology: Non-pigmented skin



Epidermal necrosis with subepidermal infiltrate

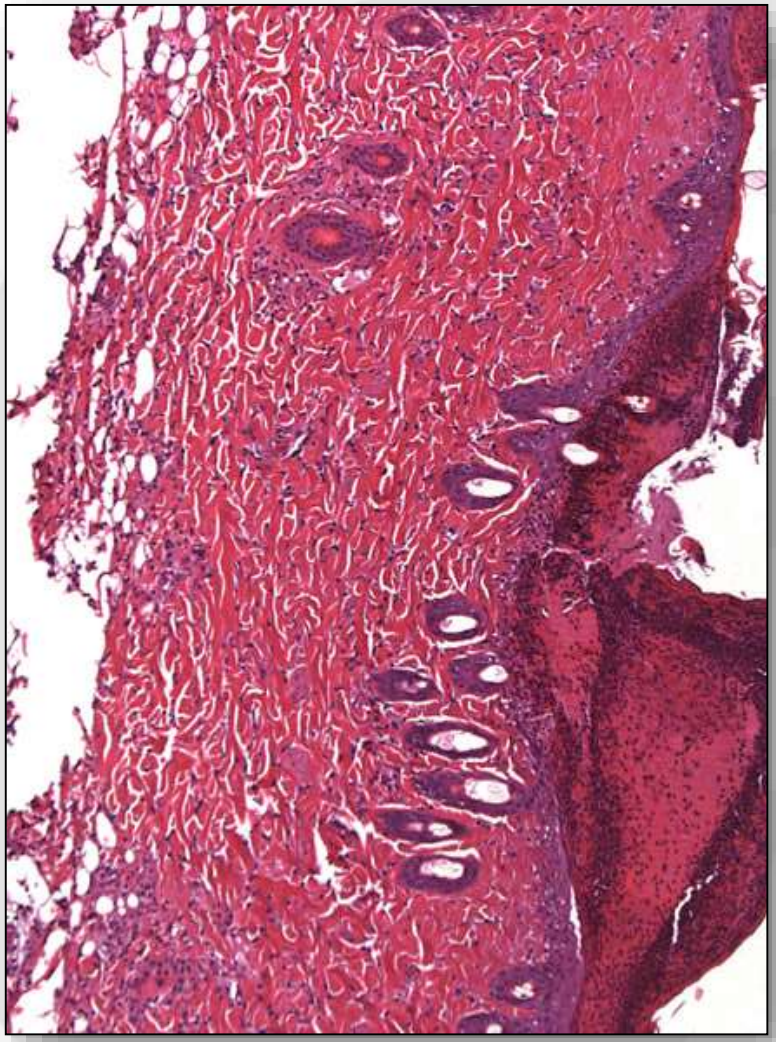


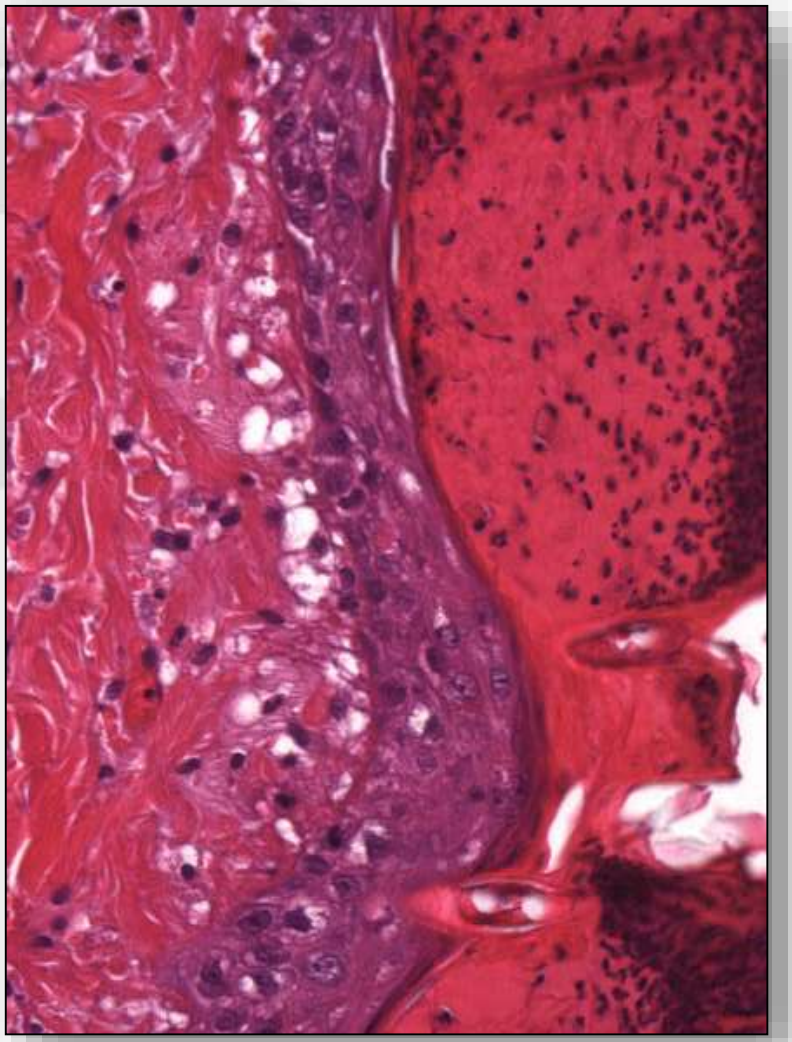
Overview on epidermal necrosis

Histopathology: Pigmented skin

Finding / Groups	1	2	Finding / Groups	1	2
Not Pigmented Skin					
Total Affected / Mean Severity	(6) F	(6) F	Total Affected / Mean Severity	(6) F	(6) F
Unirradiated			Irradiated		
Epidermal hyperplasia	0	0	Epidermal hyperplasia	6/1.7	1/2.0
Focal erosion/scab	0	0	Focal erosion/scab	0	0
Spongiosis, focal	0	0	Spongiosis, focal	1/2.0	0
Ulceration	0	0	Ulceration	0	4/2.5
Follicular inflammation	0	0	Follicular inflammation	0	5/1.4
Dermal infiltration	0	0	Dermal infiltration	4/1.3	0
Subcutaneous infiltration	0	0	Subcutaneous infiltration	1/1.0	0
Epidermal necrosis	0	0	Epidermal necrosis	2/1.0	6/3.3
Dermal inflammation	0	0	Dermal inflammation	1/1.0	6/2.7
Subcutaneous inflammation	0	0	Subcutaneous inflammation	0	6/2.0

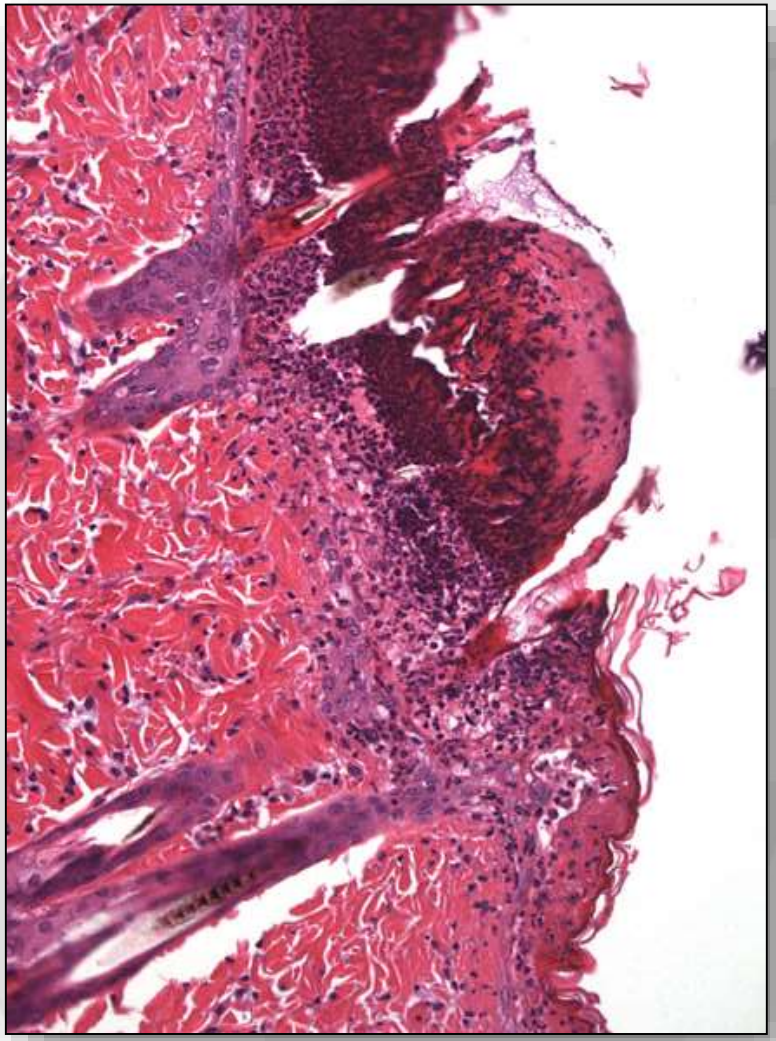
Histopathology: Pigmented skin



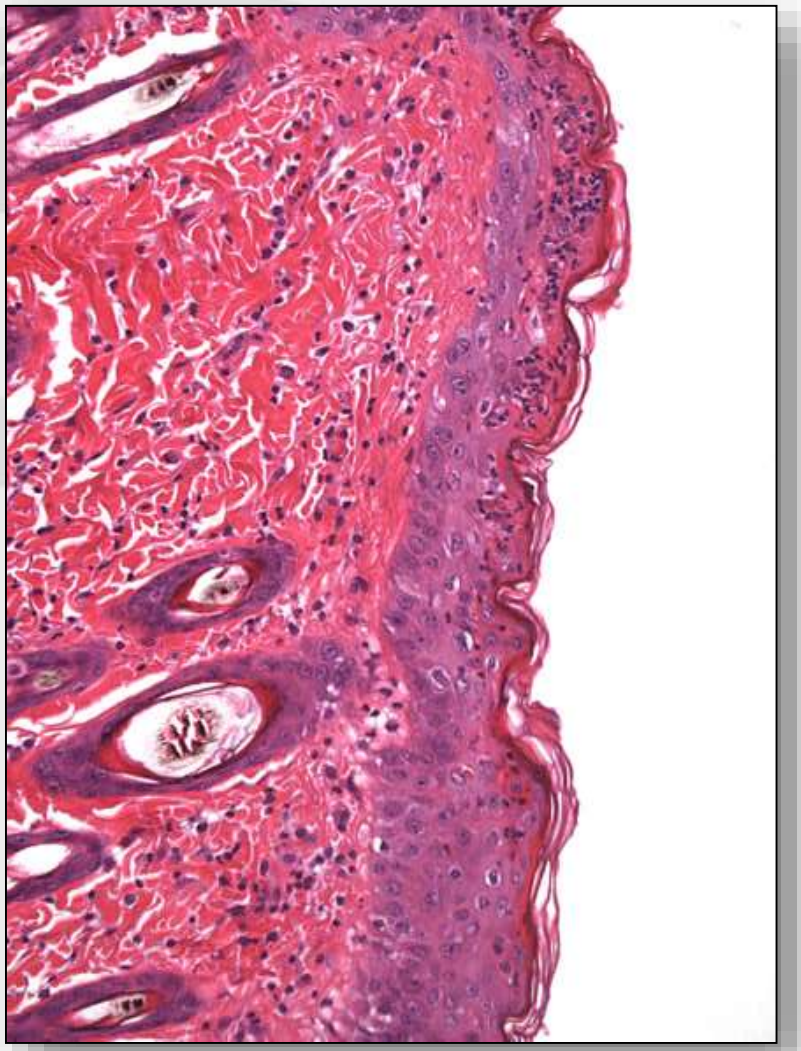


Focal erosion and scab deposition

Histopathology: Pigmented skin

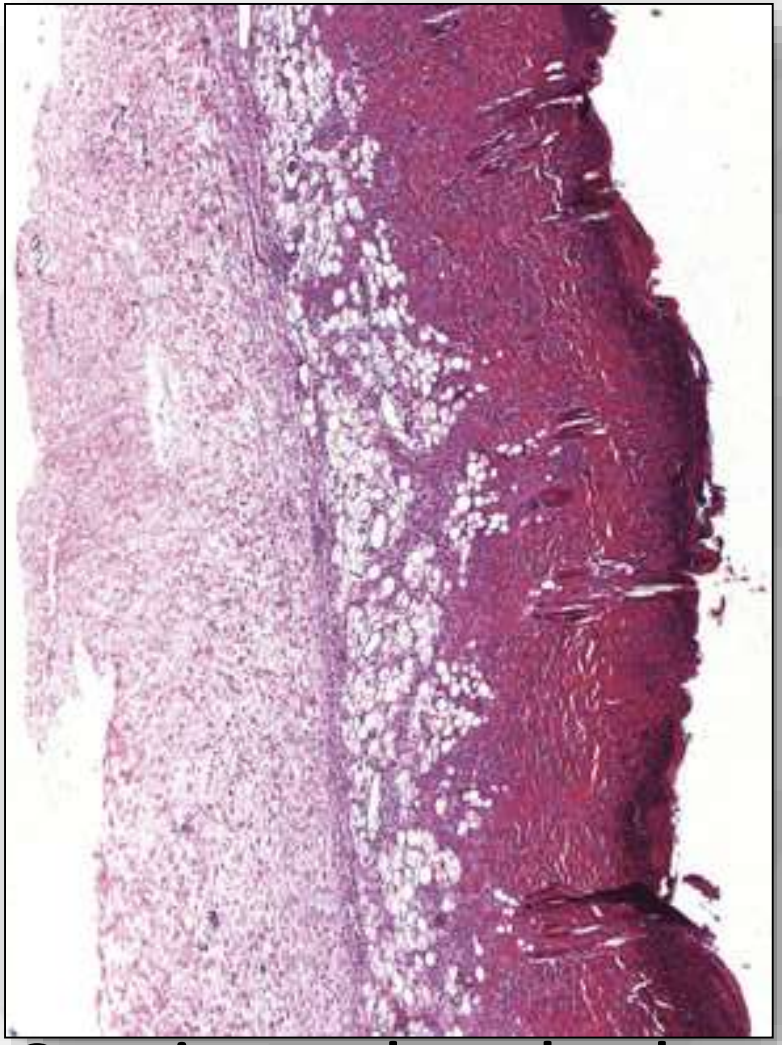


Epidermal necrosis

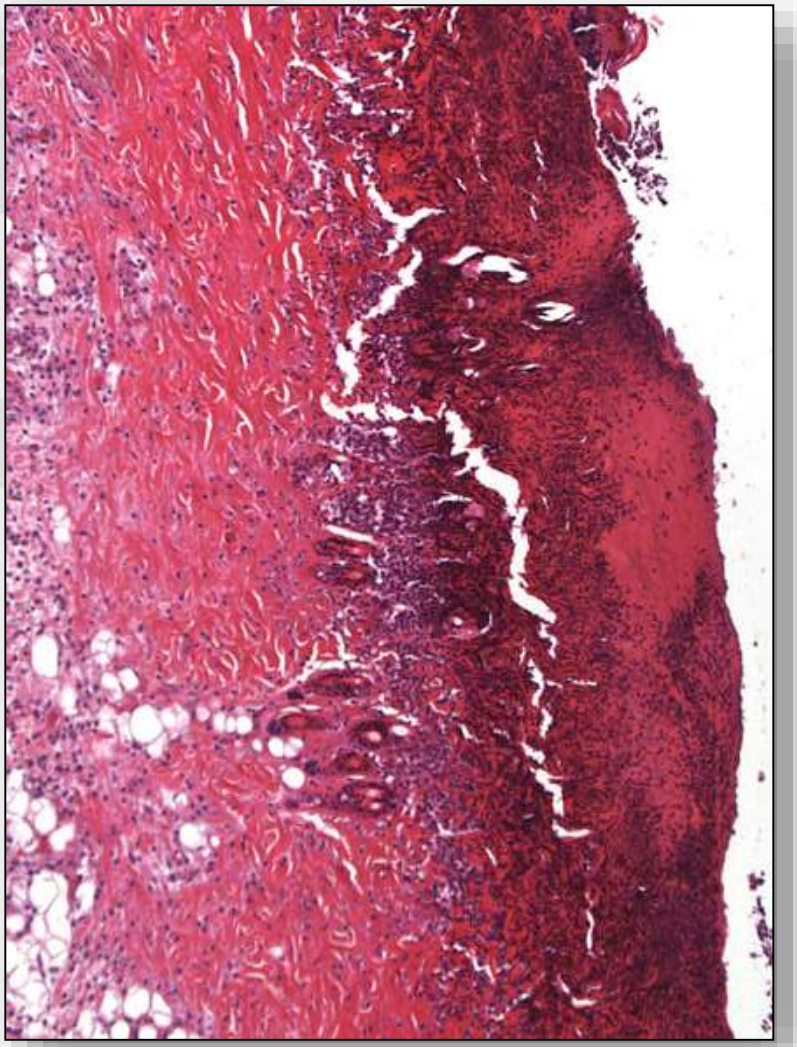


Epidermal necrosis and focal epidermal hyperplasia

Histopathology: Pigmented skin



Overview on dermal and subcutaneous inflammation and epidermal necrosis



Ulceration

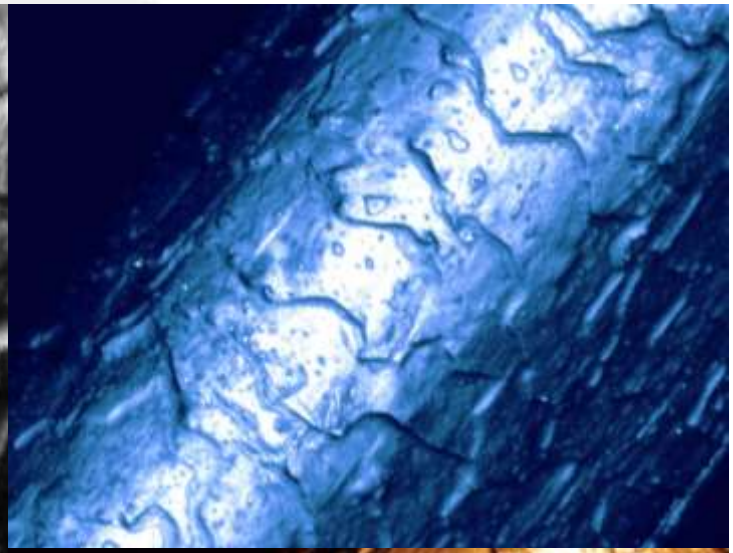
Contact allergy

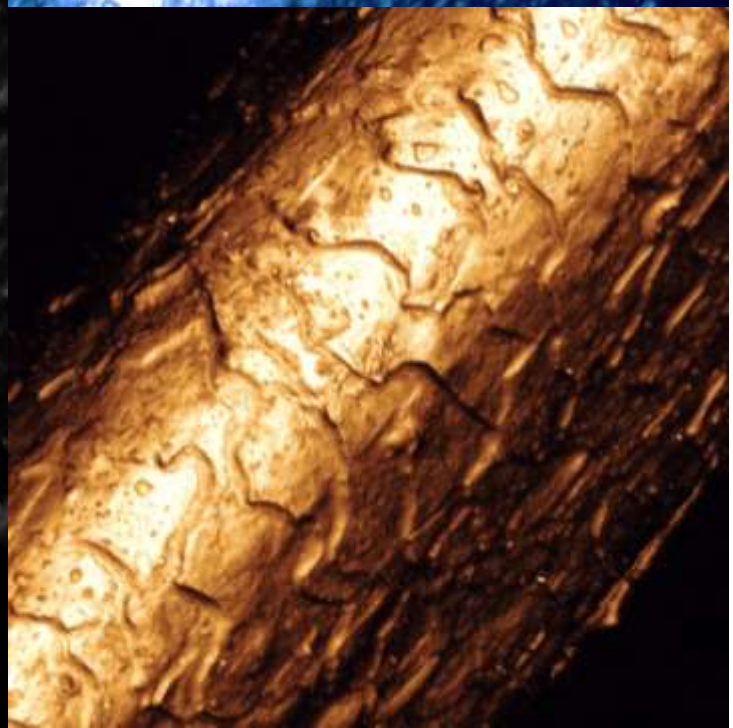
http://upload.wikimedia.org/wikipedia/commons/thumb/e/ef/Contact_with_Heracleum_sosnowskyi.JPG/220px-Contact_with_Heracleum_sosnowskyi.JPG

http://www.kidsnet.at/Sachunterricht/blu/Bild1.jpg

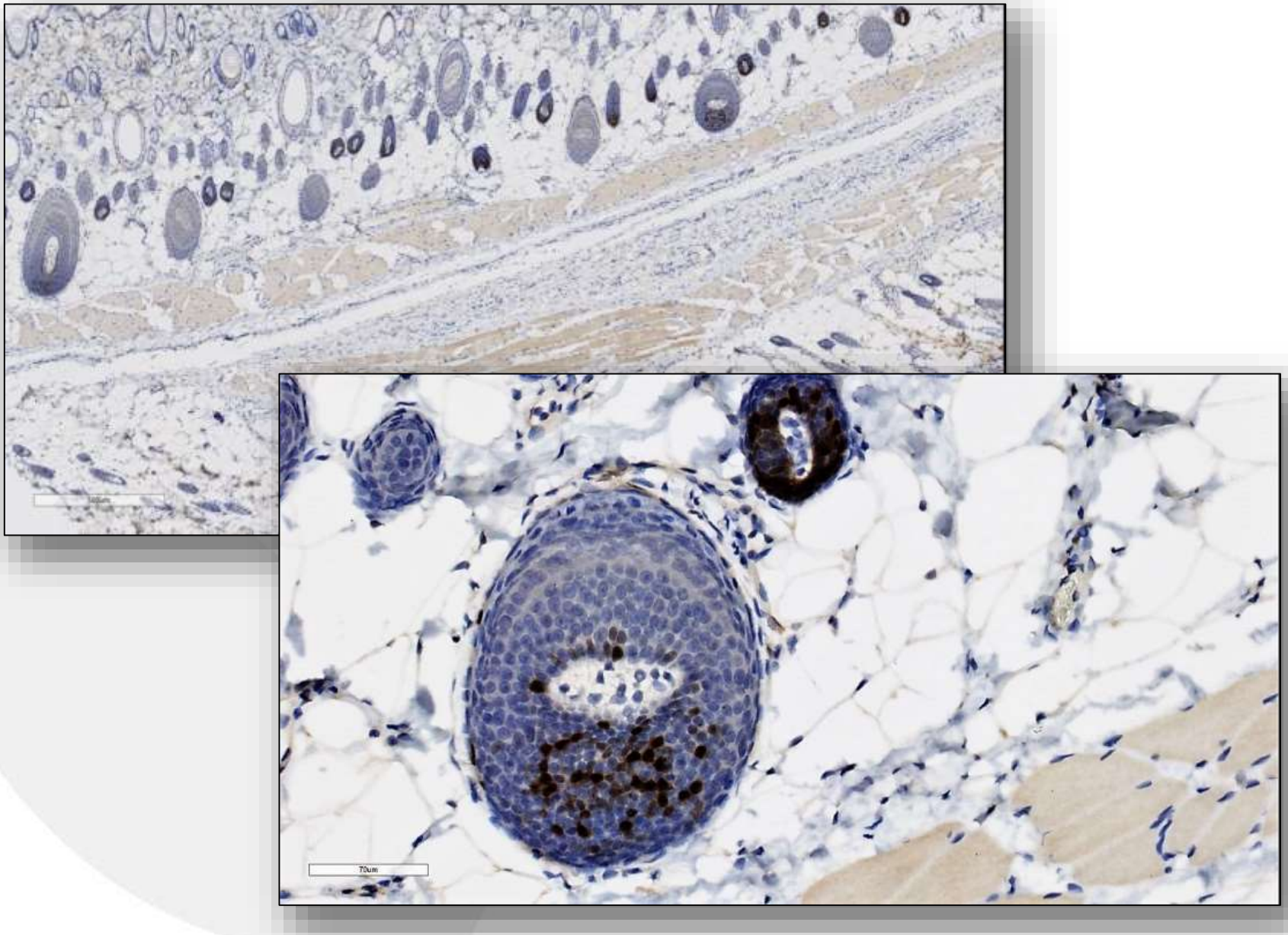
Specific Techniques

Adnexa

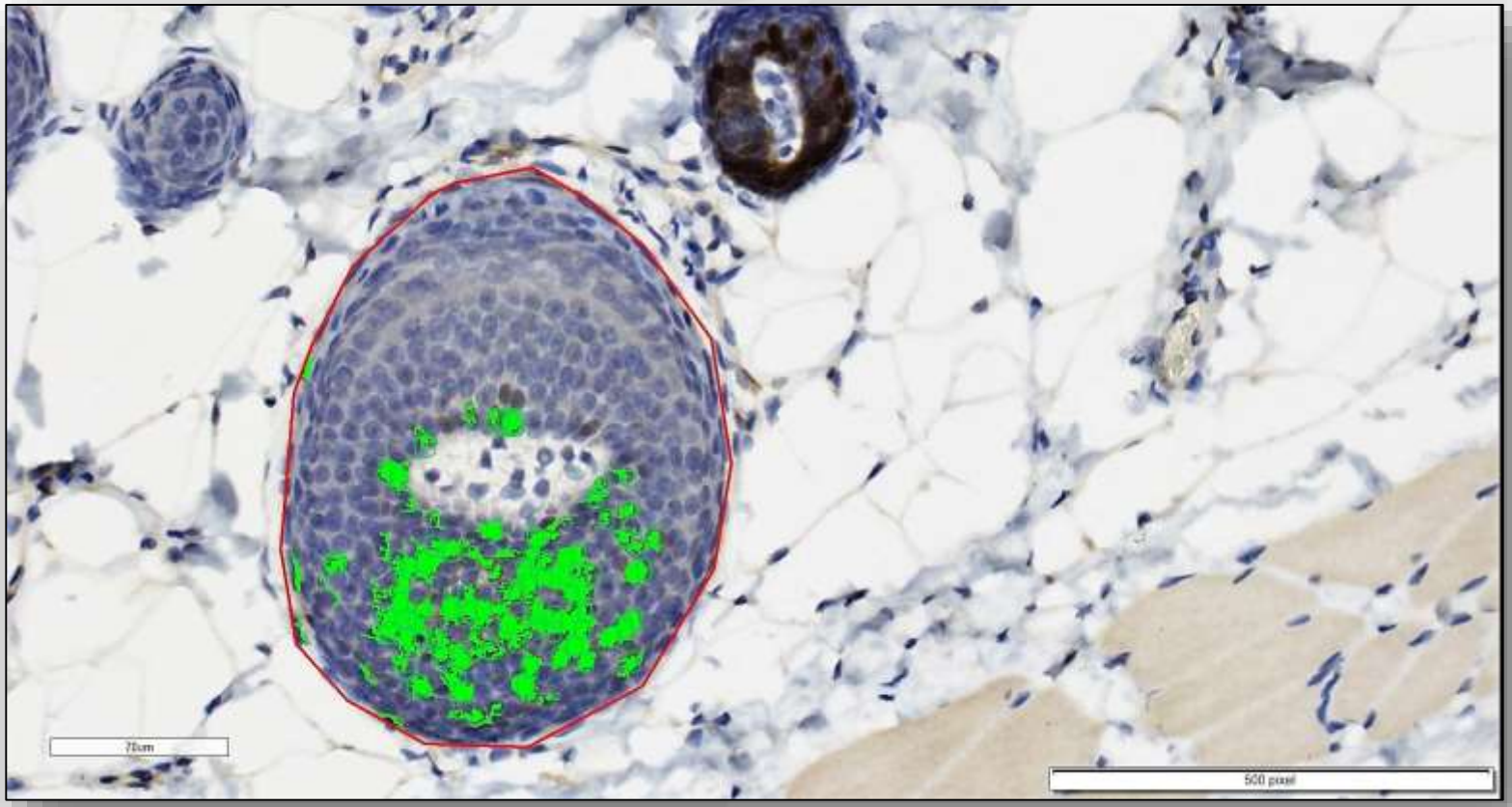




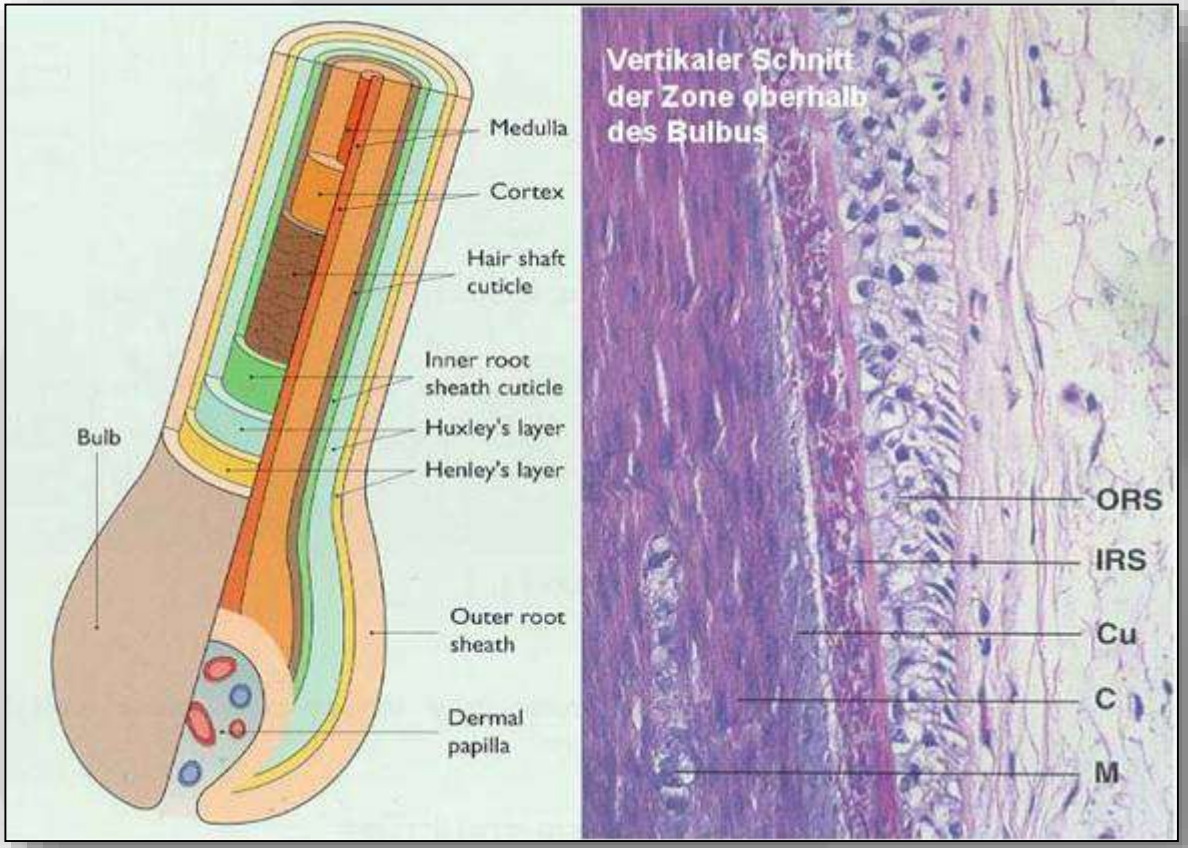
Hair follicles: IHC

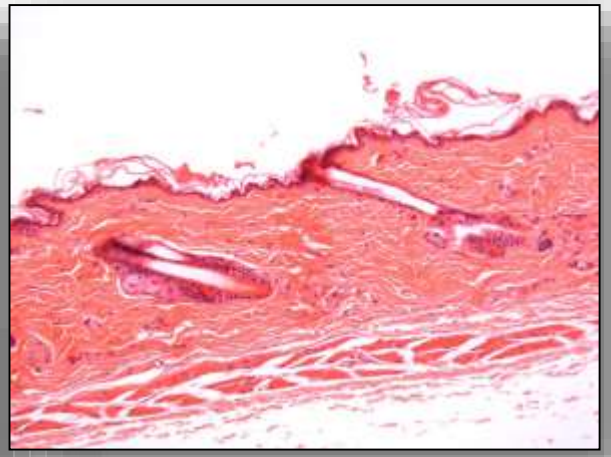


Hair follicles: IHC

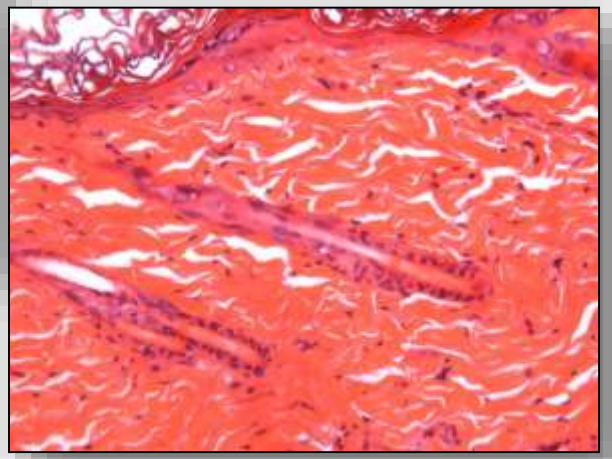


Hair



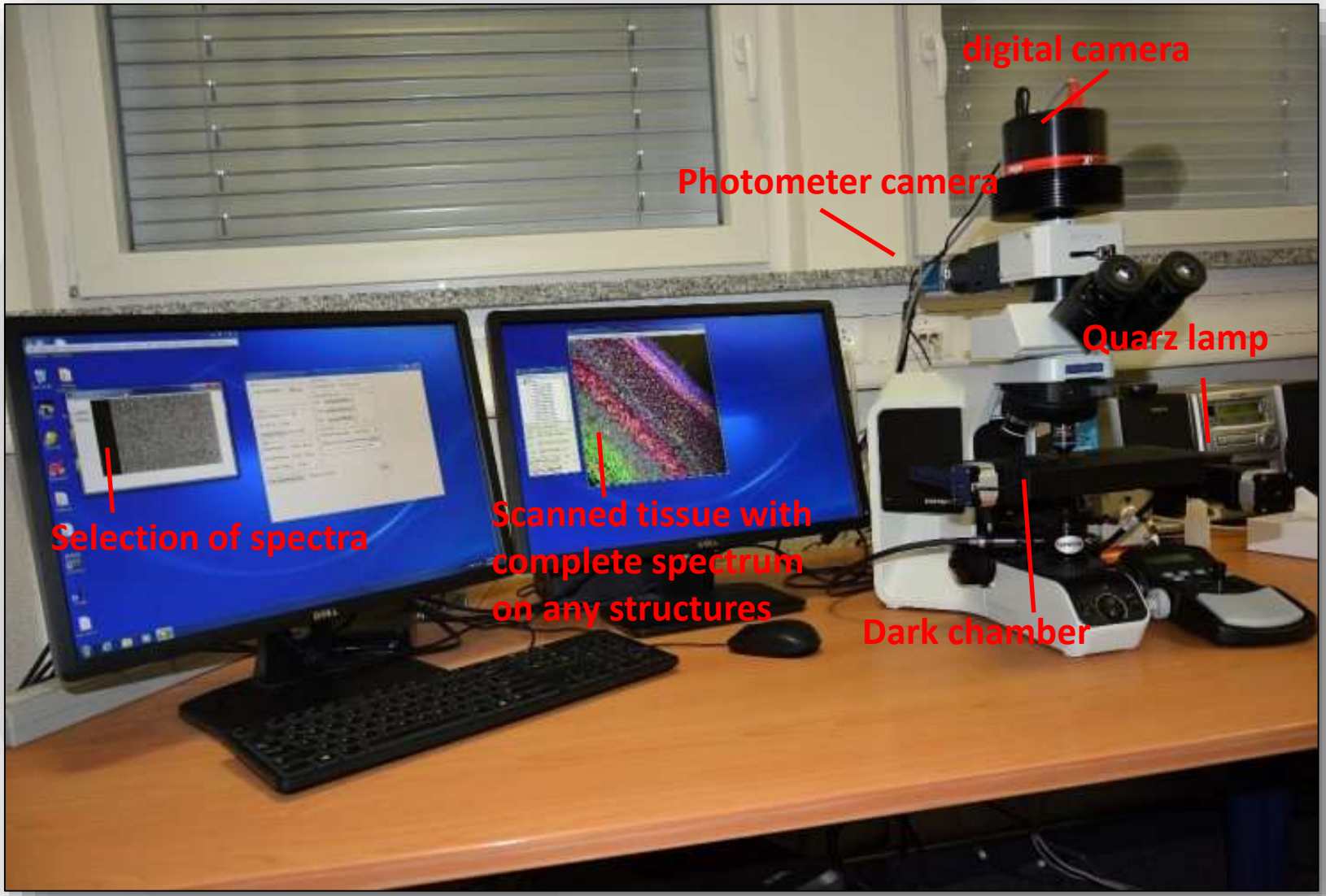


Alopecia/atrophy



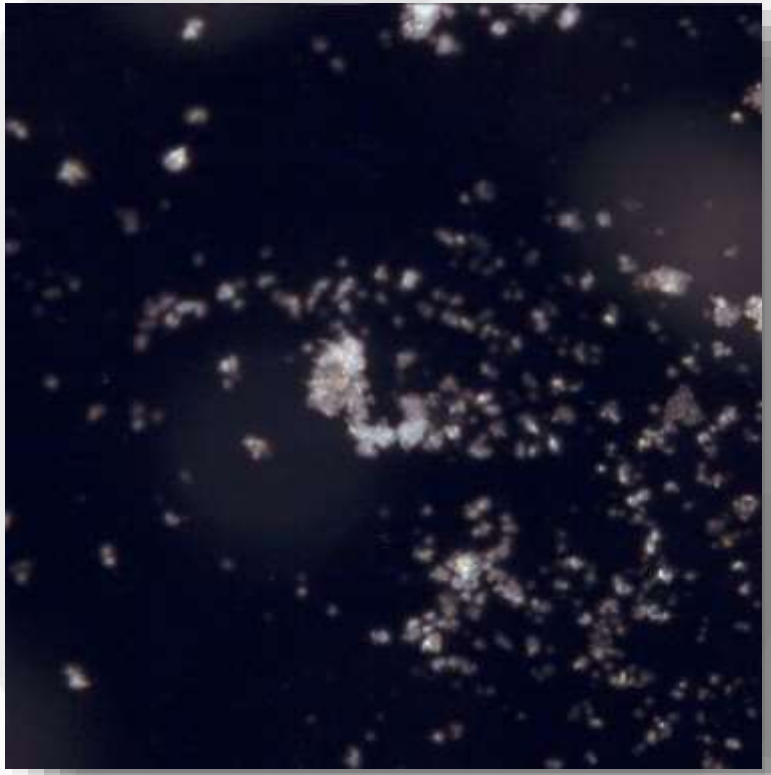
http://www.google.ch/imgres?imgurl=http://edoc.hu-berlin.de/dissertationen/auwaerter-volker-2006-01-20/HTML/image005.jpg&imgrefurl=http://edoc.hu-berlin.de/dissertationen/auwaerter-volker-2006-01-20/HTML/chapter2.html&usg)

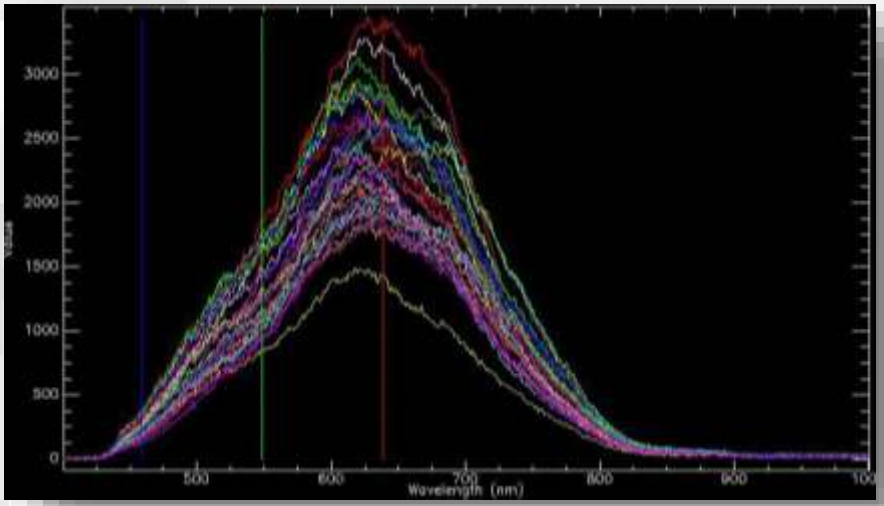
Hyperspectral Analysis



How to make it…

Dissolved Compound Y (dark field)

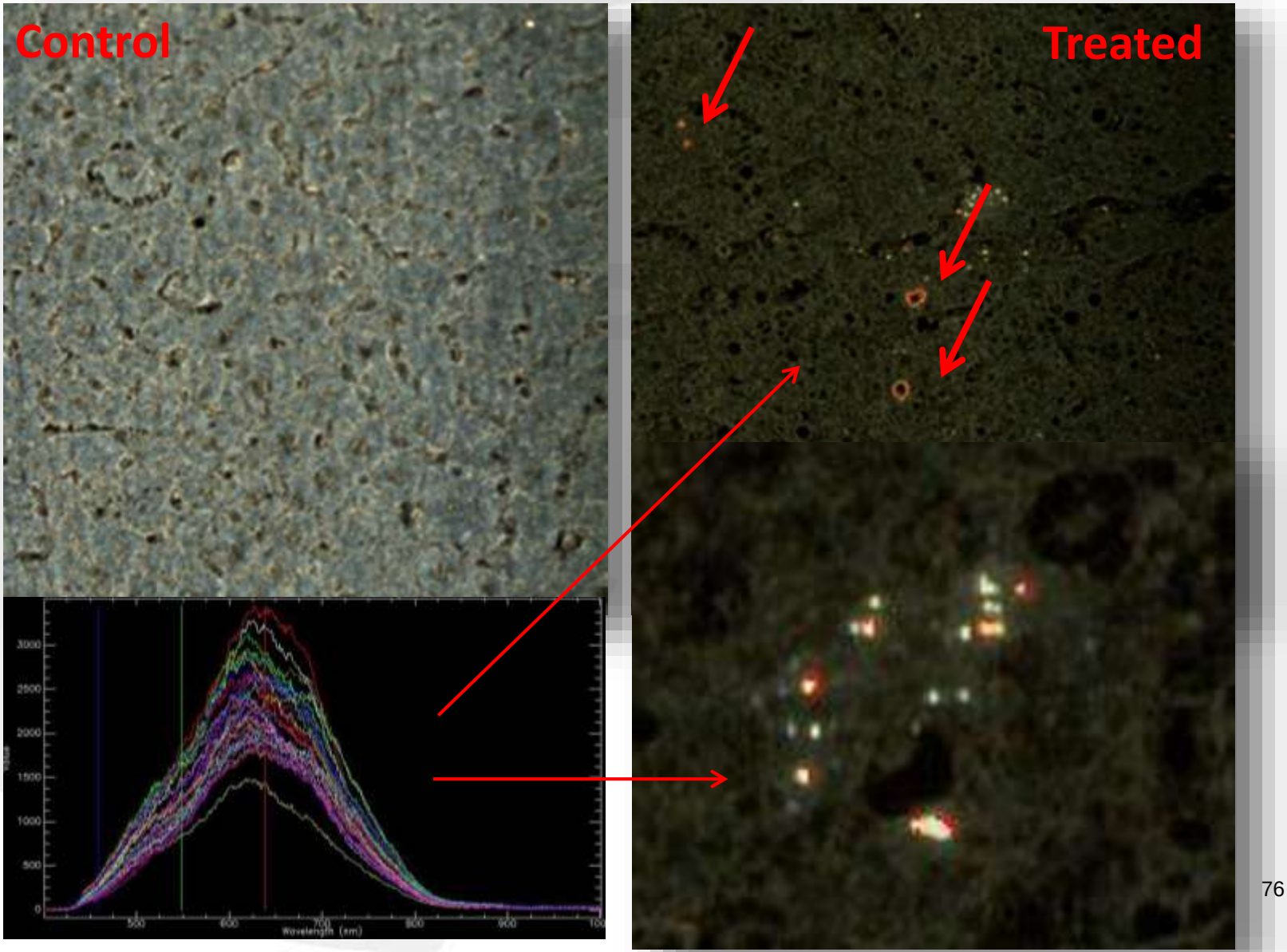




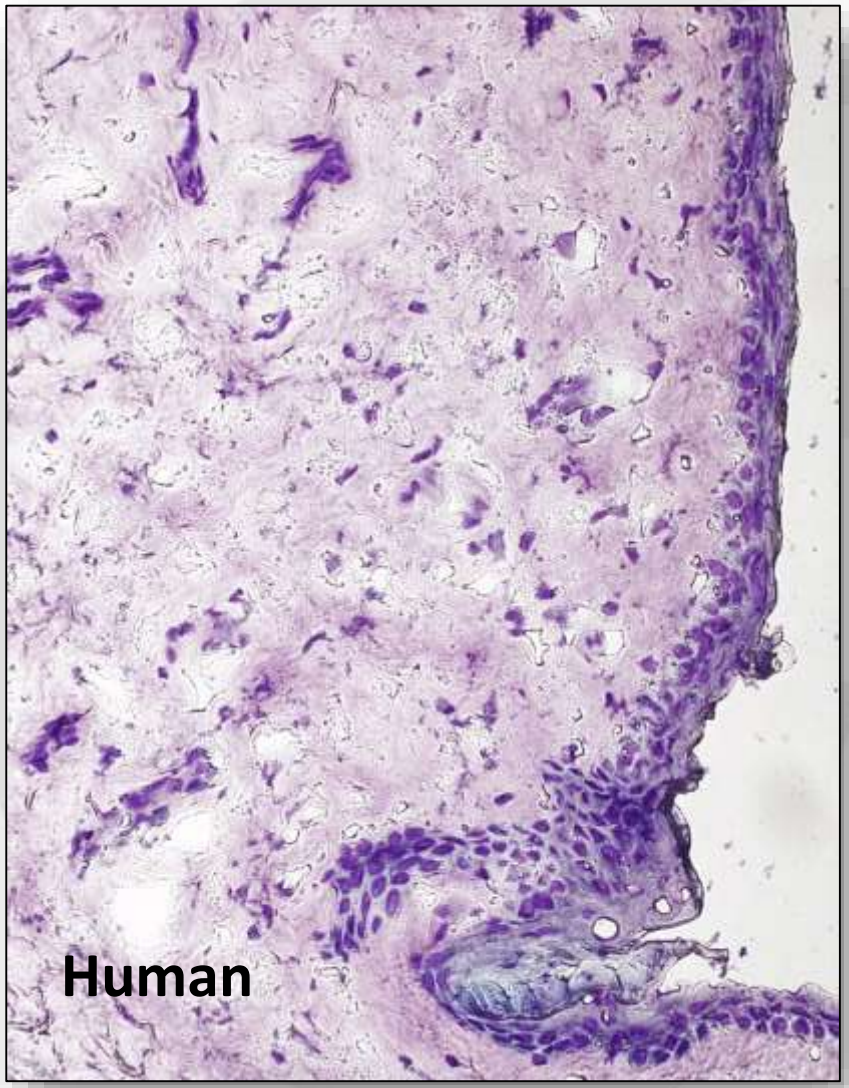
Nanoscale Hyperspectrum of test item

Weber K, Canut L, Xanxo S, Sander J, Maraschiello C, Djonov V, Yamate J, Marino K: Hepatotoxic compounds. Classic Examples in Toxicologic Pathology (4th Edition) Eds: Drommer W, Karbe E, Germann PG, 4th Edition, ISBN 978-3-9814653-0-3, 2011

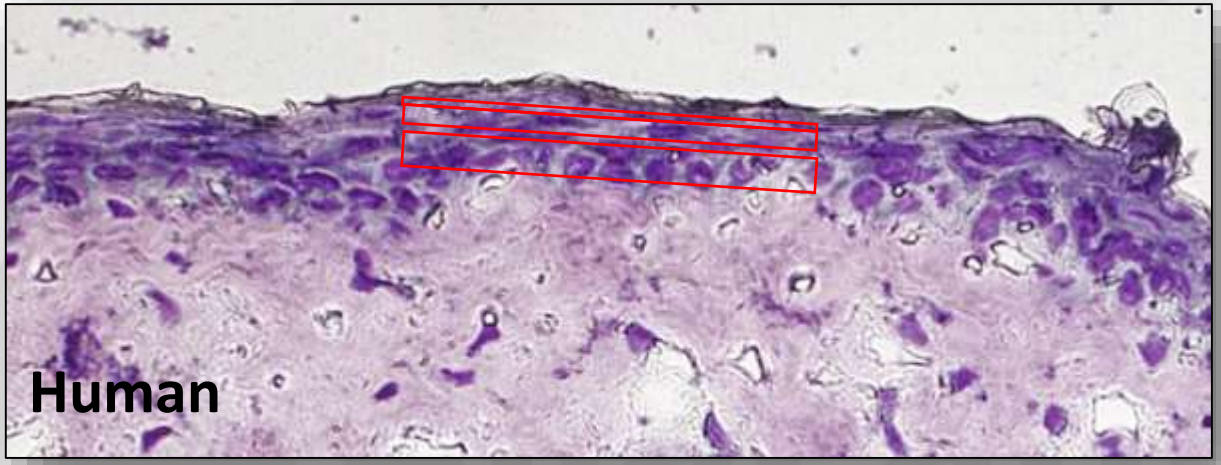
How does it looks like….

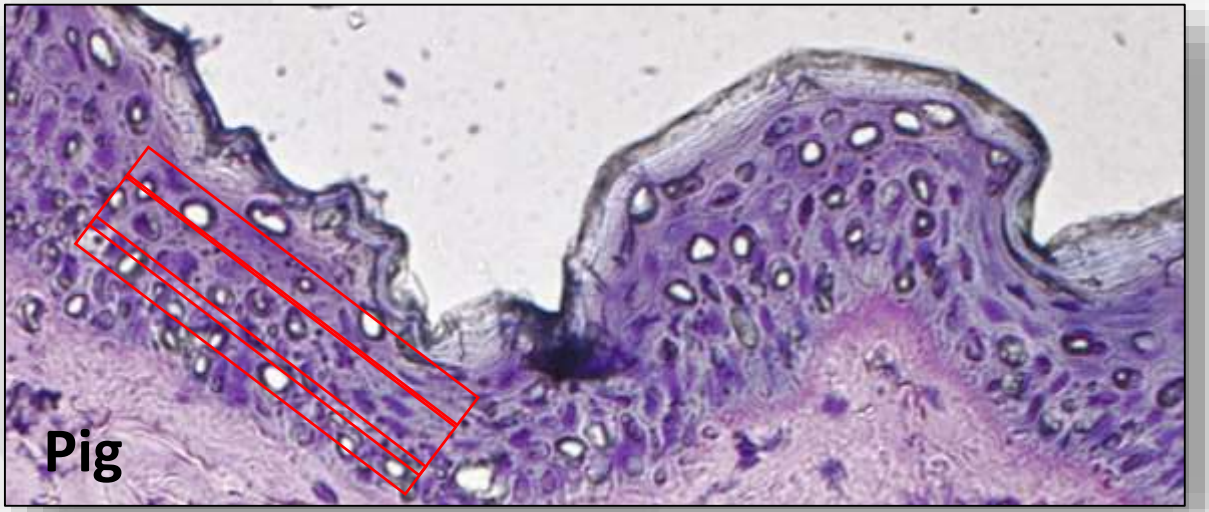


Example for Compound Tracing: Skin Samples: Giemsa, 1 min

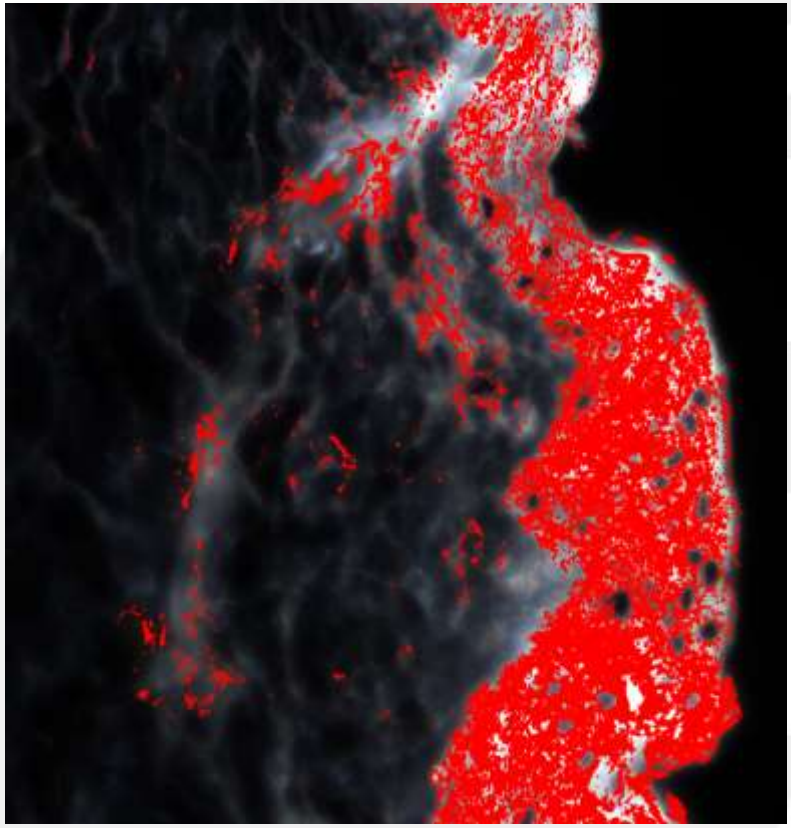


Skin: Comparison

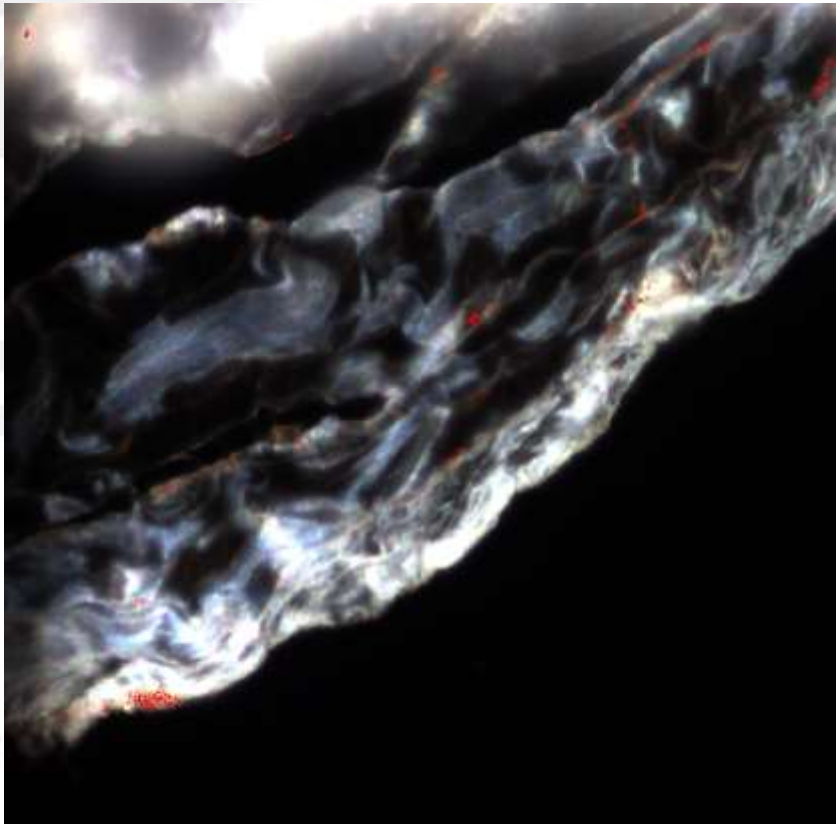




Measurements

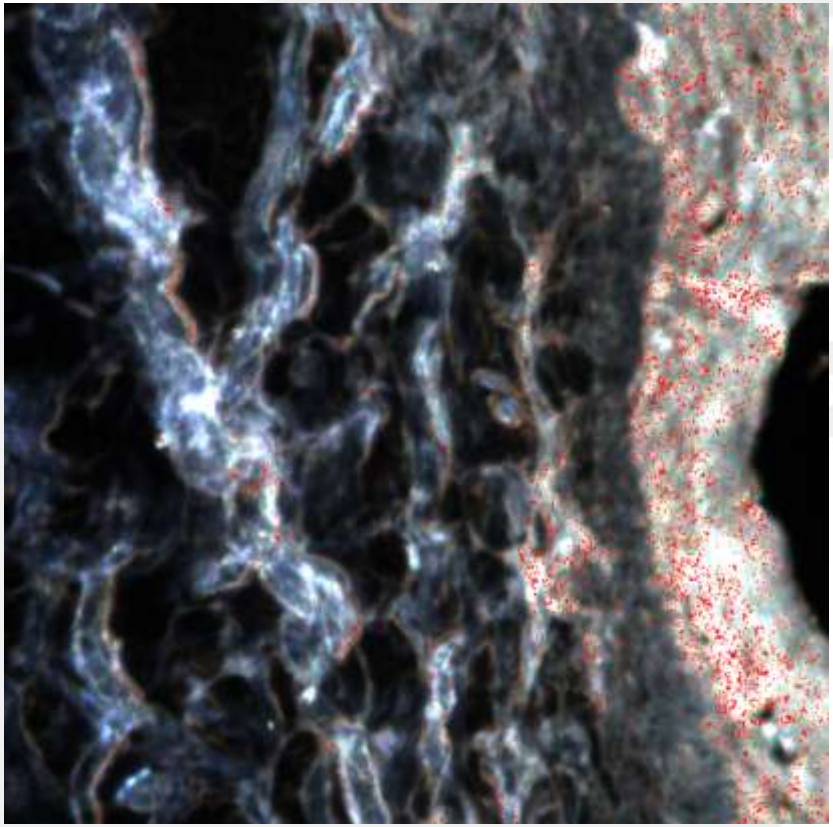


Minipig, Formulation A

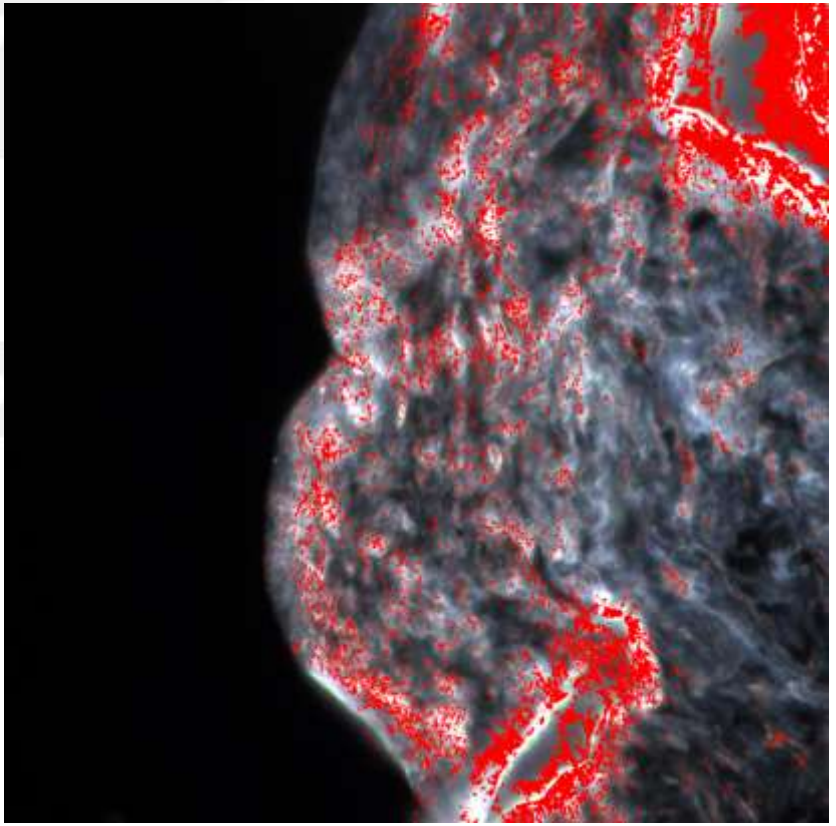


Human, Formulation A

Measurements

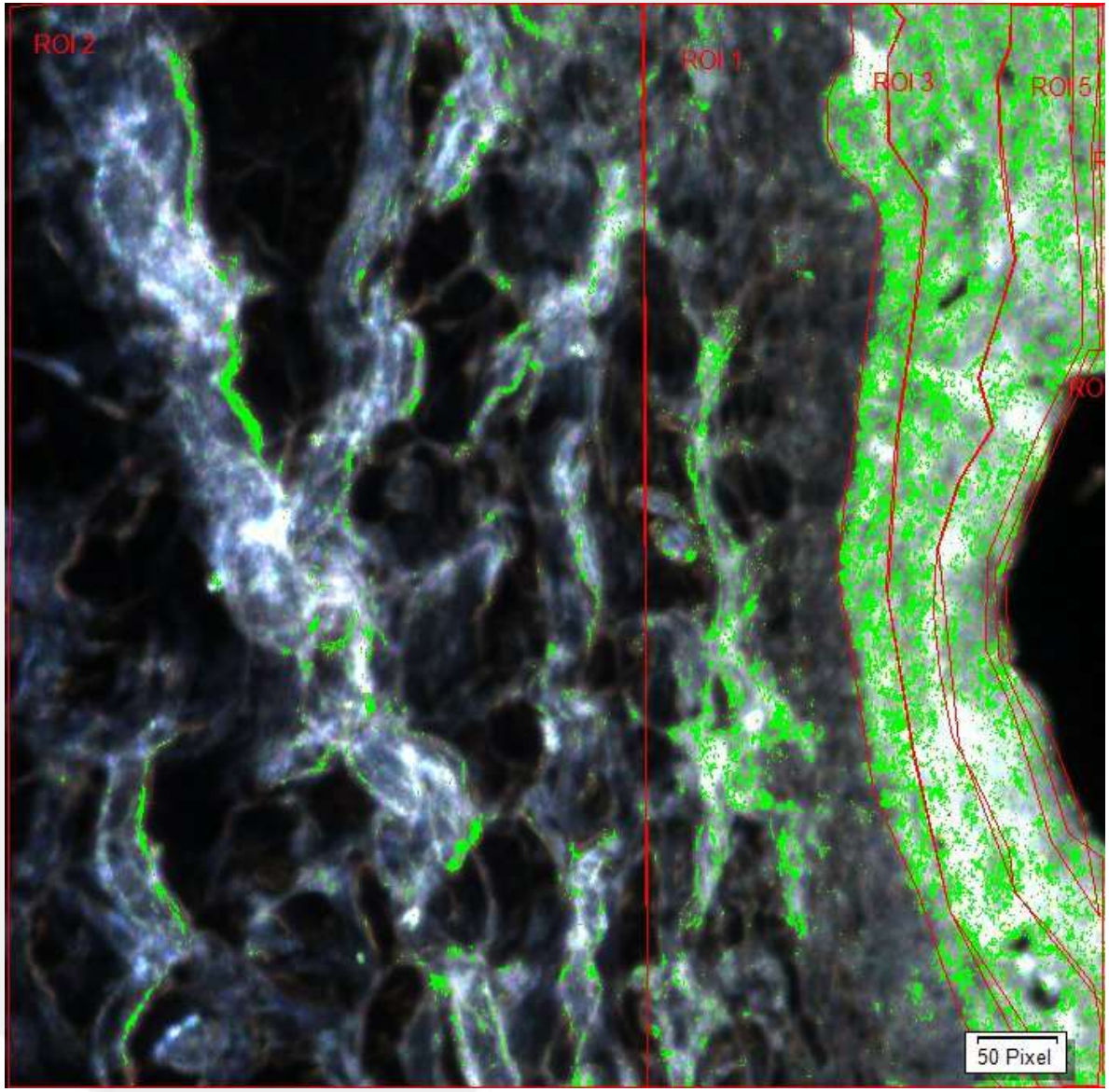


Minipig, Formulation B



Human, Formulation B

ROI‘s



ROI Print for measurements

Statistik	Objektflächenanteil (%)	ROI	ROI-Fläche (Pixel²)	ROI
		1.77	276429	ROI 2
		14.78	199645	ROI 1
		48.56	19990	ROI 3
		41.93	32743	ROI 5
		29.37	31260	ROI 4
		35.25	8877	ROI 6
Anzahl		6	6	

ROI 1: Stratum papillare } Corium
ROI 2: Stratum reticulare }

ROI 3: Stratum basale } germinativum } Epidermis
ROI 4: Stratum spinosum }

ROI 5: Stratum granulosum } mortificatium }
ROI 6: Stratum corneum }

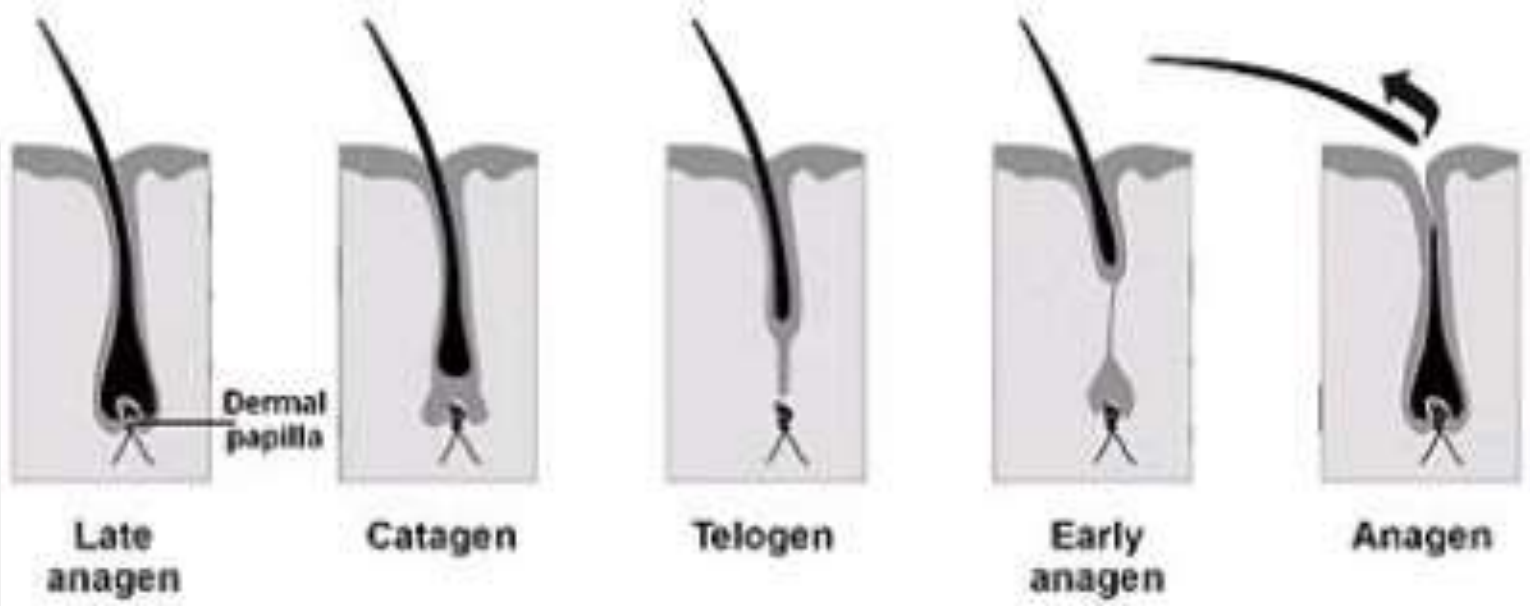
Alopecia Under Treatment

Hair follicles are not all in the same phase at the same time point

Different morphology include:

- **Anagen: bulbs of hair follicles more closely associated with adipose tissue than they are in telogen due to the deeper penetration of the follicles into the subcutaneous tissue during anagen**
- **Telogen: dermal papilla is separated from the hair club, but remains in close proximity to it, whereby there is no connecting stalk (Al-Bagdadi FK et al., 1979).**

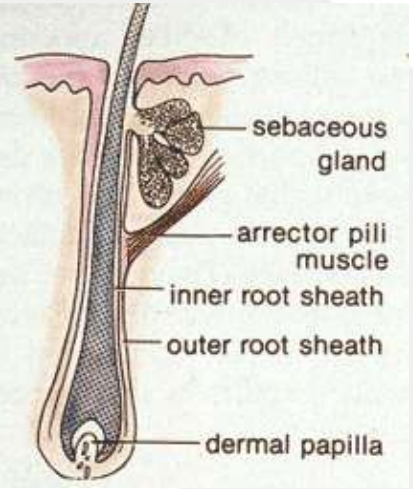
Follicle stages



http://www.google.ch/imgres?imgurl=http://www.hshairclinic.co.uk/_images/hair_growth_cycle.jpg&imgrefurl=http://www.hshairclinic.co.

Anagen

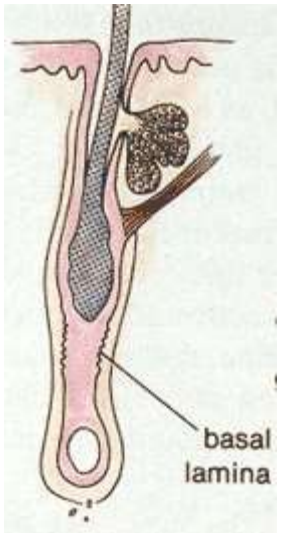
- **Generation of outer sheath, inner sheath and hair**
- **Mature anagen follicle consisting of upper and lower segments**
- **Fully developed: follicle envelops largely a follicular papilla and consists mostly of matrical material**
- **Early phase: new follicular germ at base of isthmus. New elongated germ whose arc-like base is contiguous with a discrete follicular papilla.**



http://www.medscape.com

Catagen

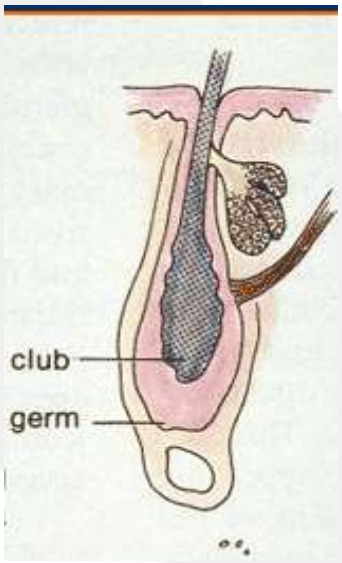
- **Lower segment of follicle shrivels into thin cord of epithelia (followed upward along a fibrous track)**
- **Early catagen: follicular bulb is no longer extent**
- **Advanced catagen: lower segment of involuting follicle consists of column of epithelial cells surrounded by thickened basement membrane. Residues of ill-formed follicular papilla at base of column.**
- **End stage: follicular papilla is not recognizable as a discrete structure.**



http://www.medscape.com

Telogen

- **Ill-defined follicular papilla reposes immediately beneath the isthmus (ready for initiating the follicular cycle anew)**
- **Follicle consists only of upper segment. Columnar cells aligned in a palisade. At base of isthmus remainders of follicular papilla.**



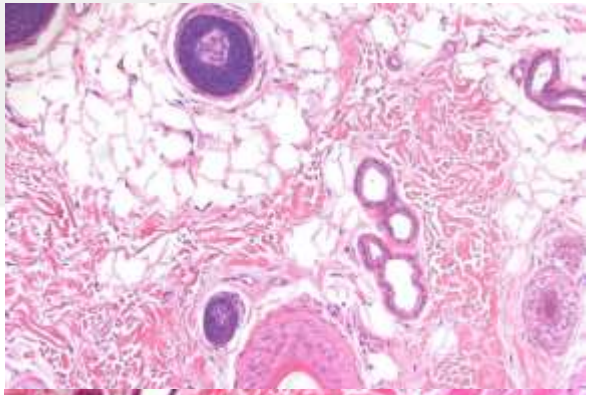
http://www.medscape.com

Situation in regular skin samples

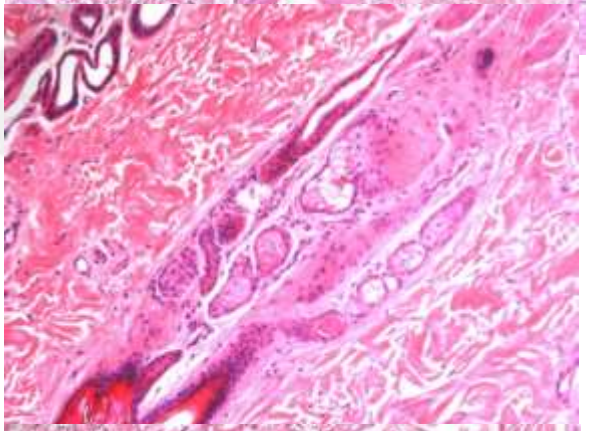
- **major follicle type in different growing phase**
- **follicle phase can be differentiated per sample into anagen, telogen or catagen.**
- **in cases, where there were similar portions of several phases present, all phases should be reported**
- **Example (normal skin samples)**

Situation in regular skin samples

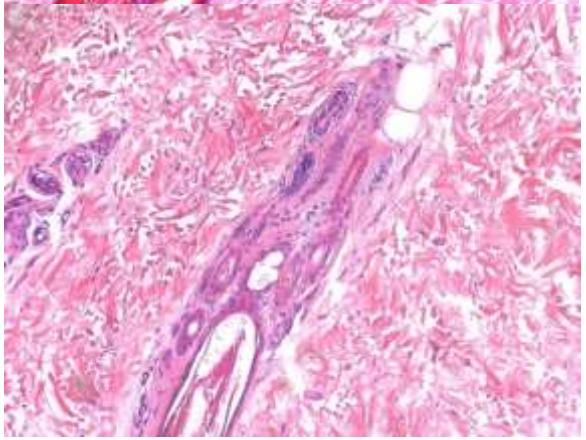
Mainly anagen hair



Mainly telogen hair



Mainly catagen hair



Situation in regular skin samples

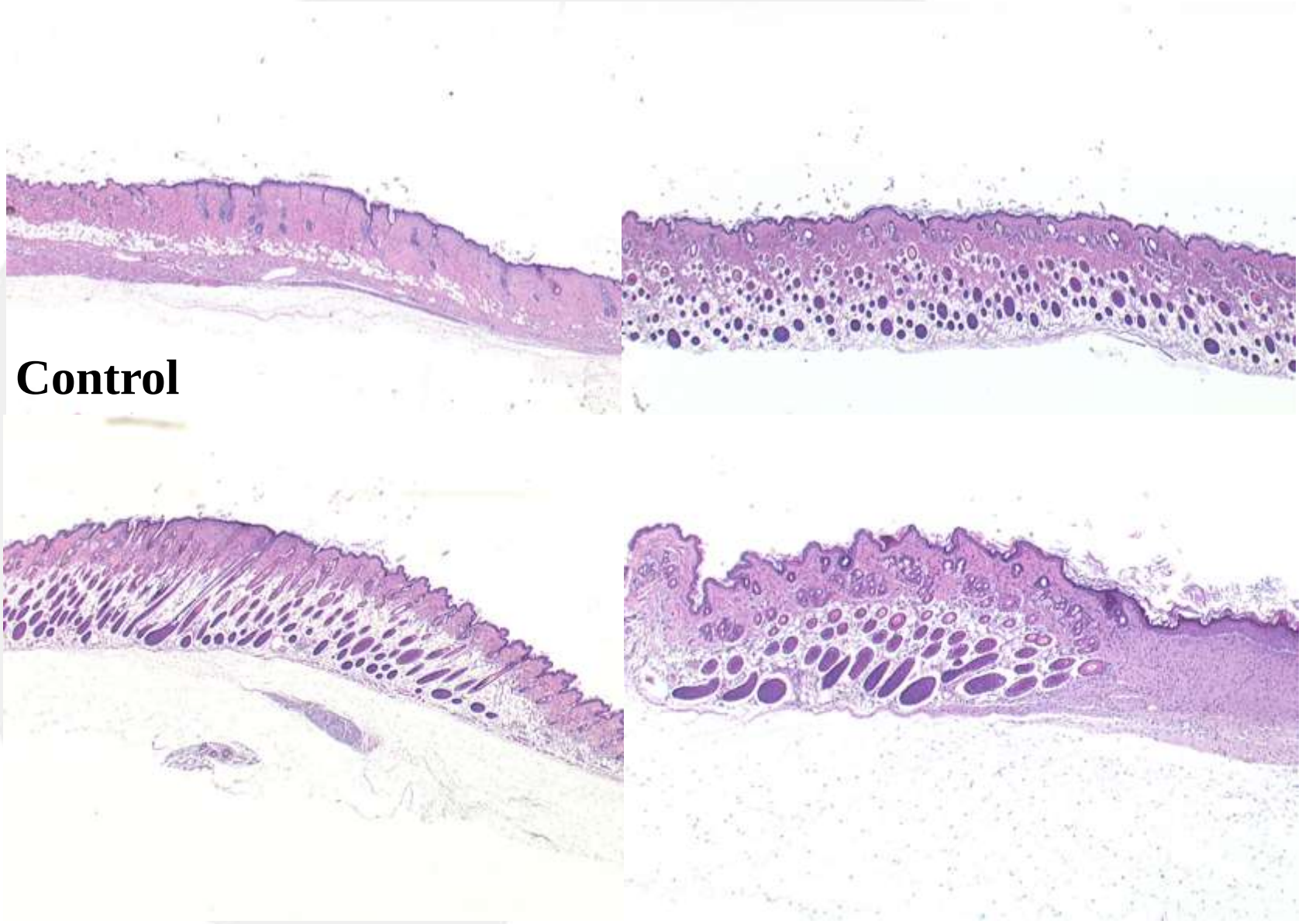
Normal skin samples:

Finding/Groups:	1		2		3		4	
Number of animals Total Affected	6 M*	6 F	4 M	4 F*	4 M	4 F	6 M	6 F
Anagen	2	-	3	-	1	1	-	-
Anagen – Telogen	3	2	-	1	2	2	4	2
Telogen	-	4	-	1	1	1	1	3
Telogen – Catagen	-	-	1	1	-	-	-	1
Catagen	-	-	-	-		-	1	-

Gross lesion skin samples:

Finding/Groups:	1		2		3		4	
Number of samples Total Affected	1 M	9 F*	1 M	3 F	5 M	6 F*	40 M*	41 F*
Anagen	1	4	-	1	-	1	4	5
Anagen – Telogen	-	4	-	-	1	2	18	10
Telogen	-	-	1	2	4	2	14	24
Telogen – Catagen	-	-	-	-	-	-	1	-
Catagen	-	-	-	-	-	-	1	1

Hypertrichosis, mouse (Ca-agonist, s.c.)

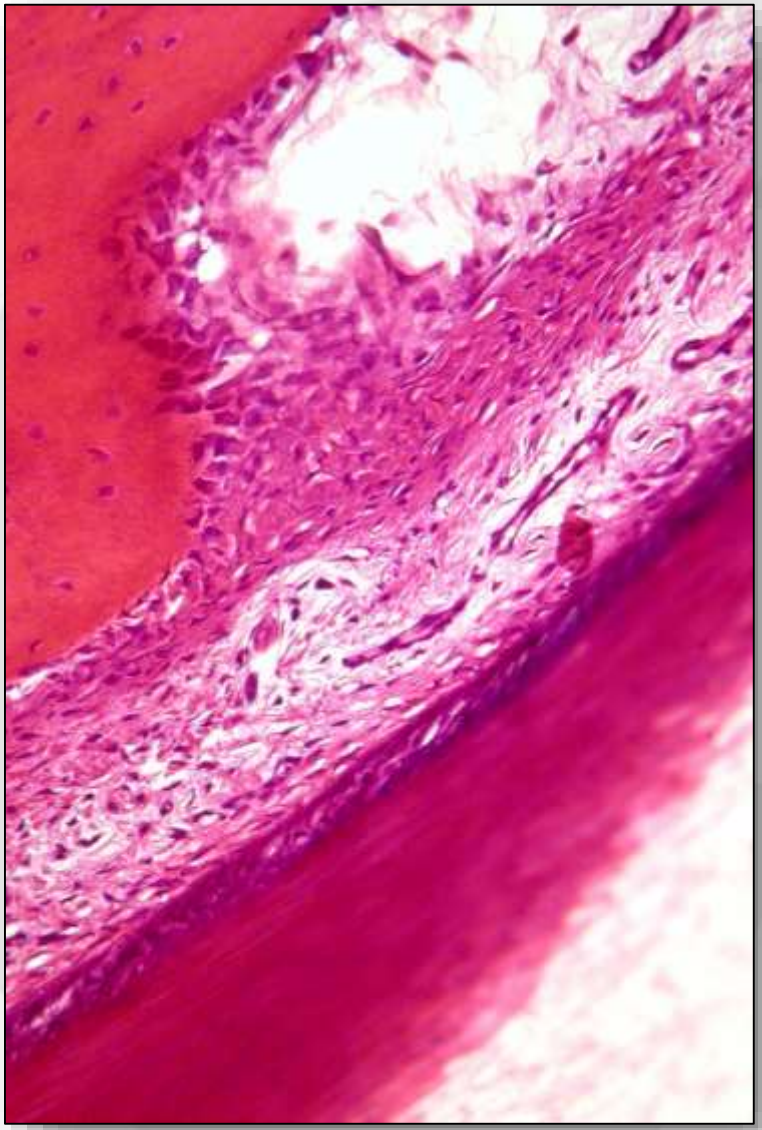


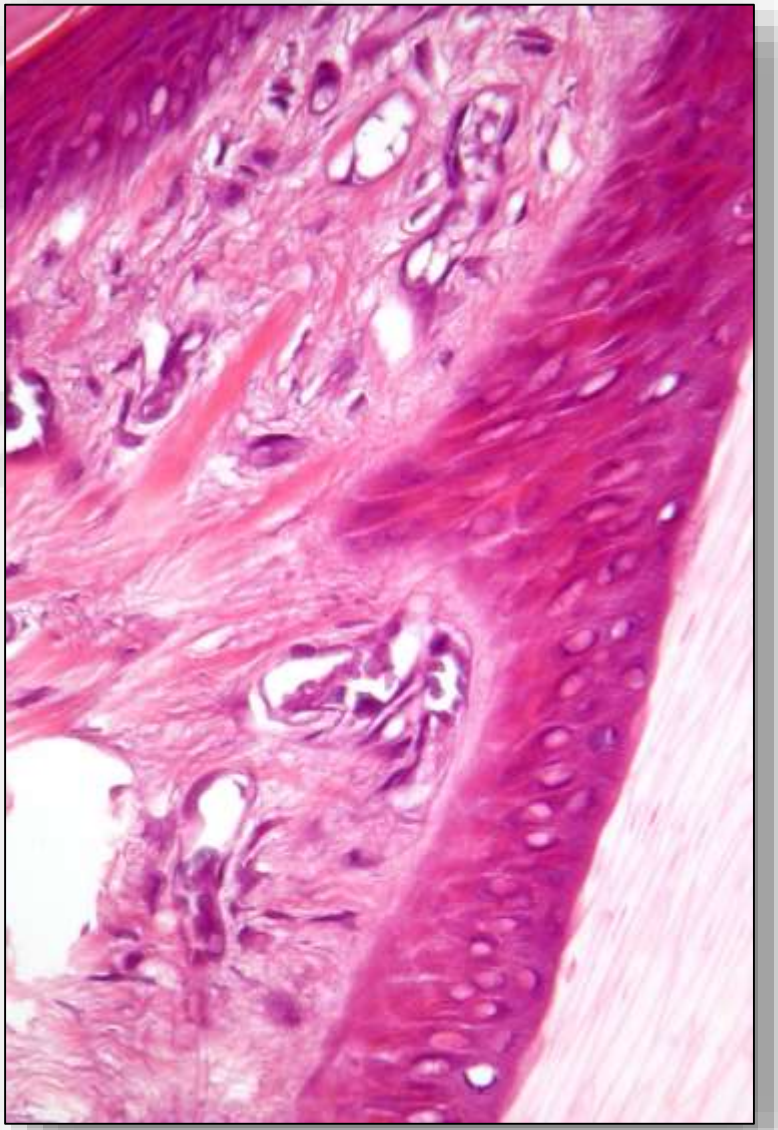
Anaphylaxis, domestic pig

Nails: Rat

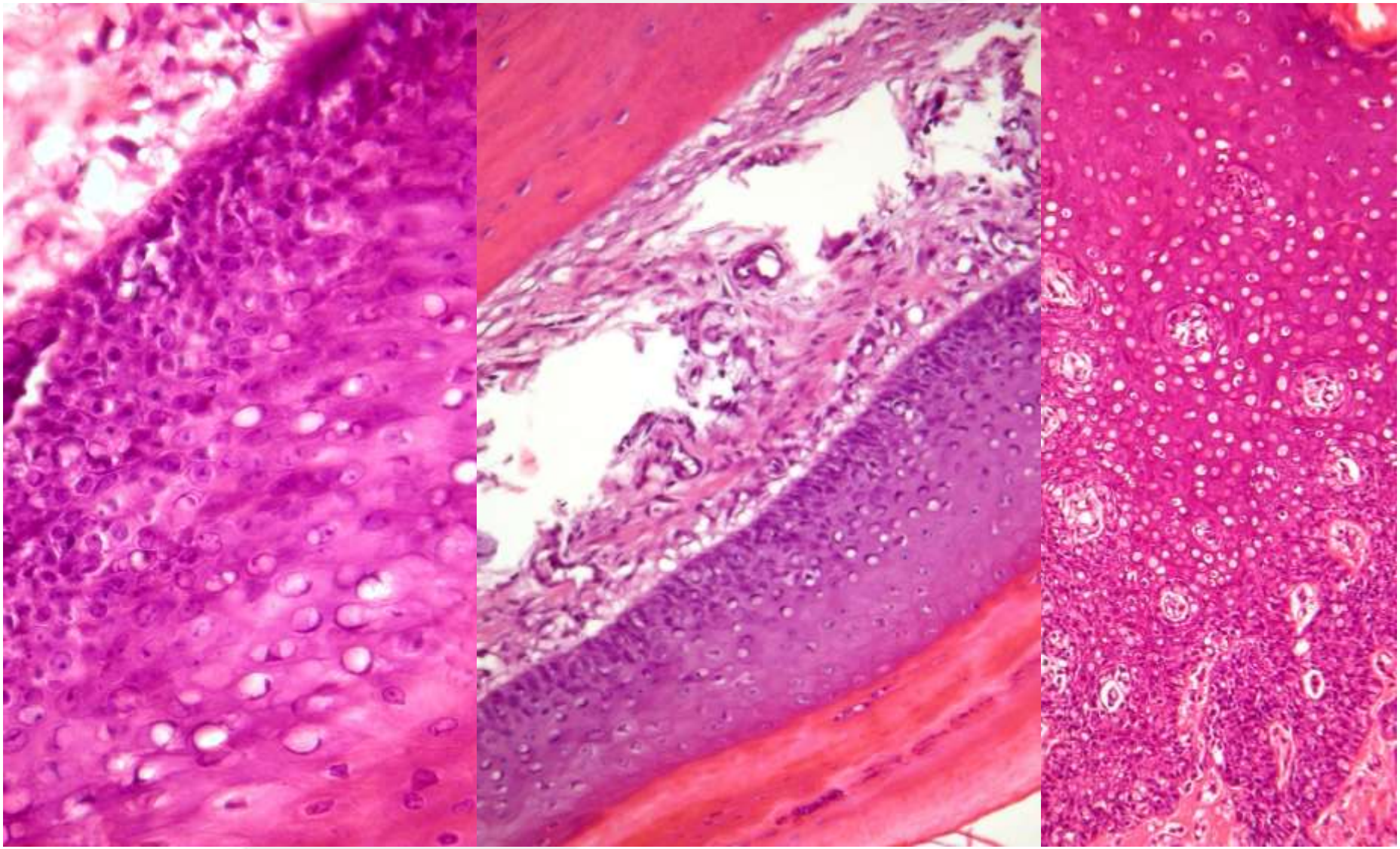
Zaias N (2013). The Nail Bed, Part I. The Normal Nail Bed Matrix, Stem Cells, Distal Motion and Anatomy. J Dermatolog Clin Res 2(1): 1008.

Nails

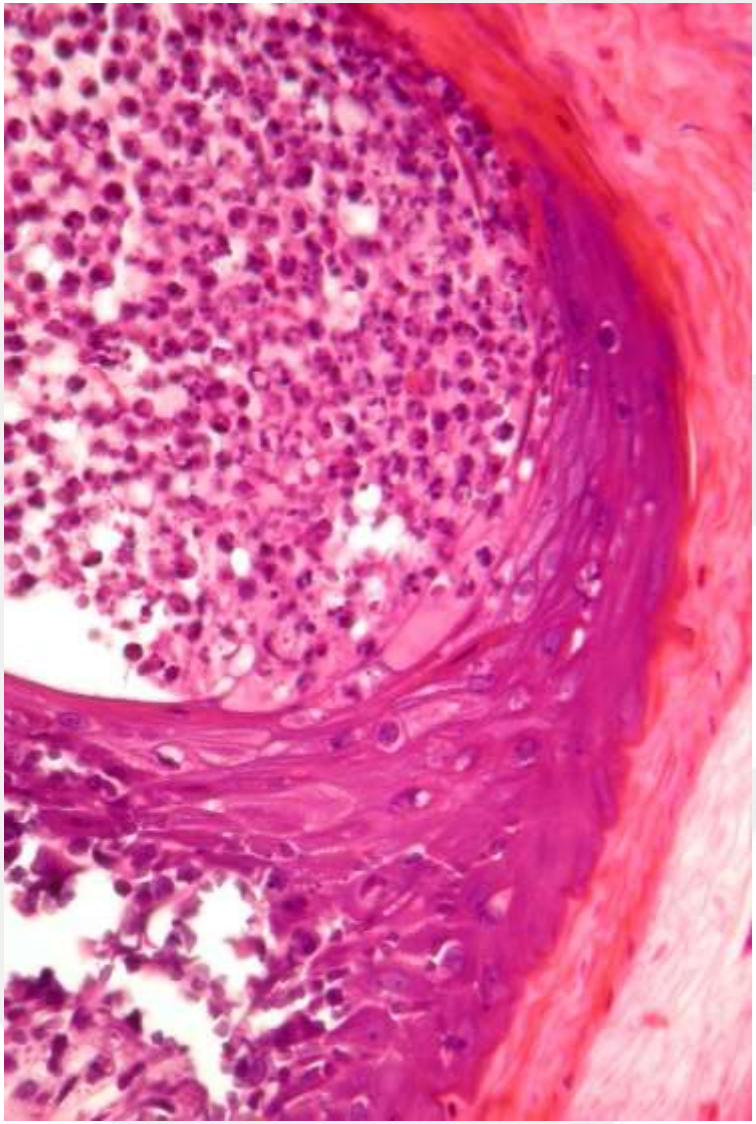


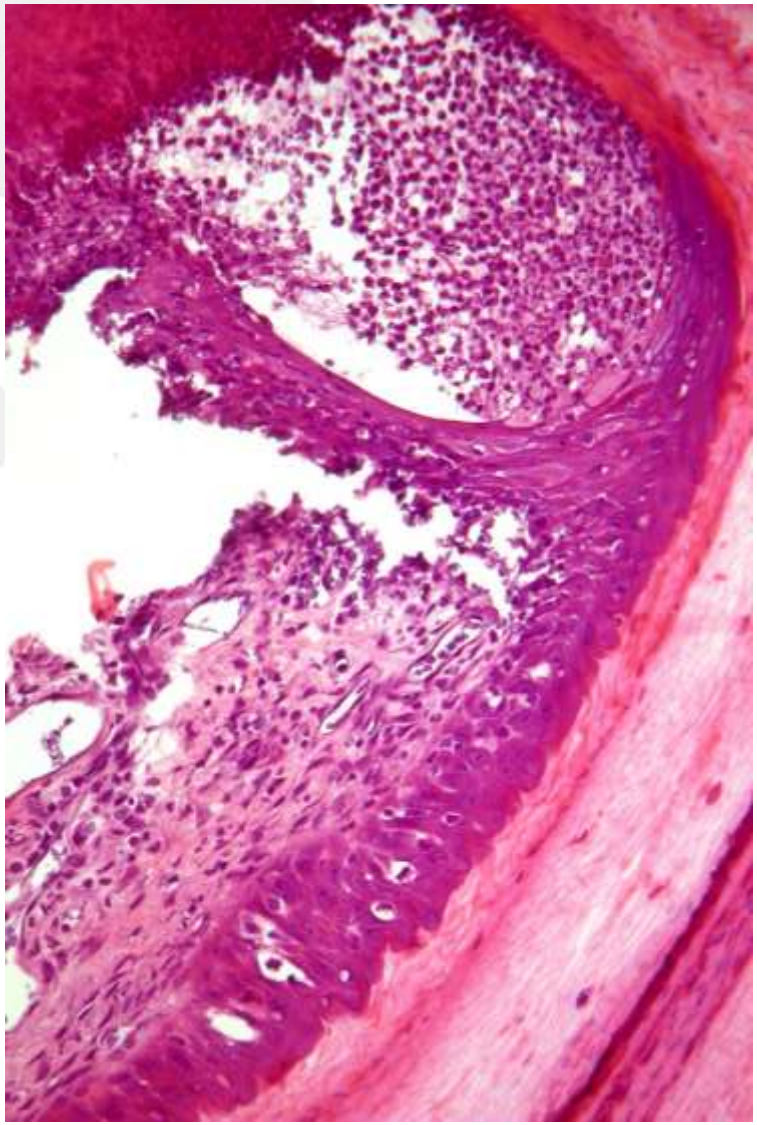


Nail with induced lesion (immunotherapeutics)



Nail with induced lesion (immunotherapeutics)






Litoptena