difference in CK117 expression between different stages in skin or in cases with large cell transformation.
Conclusion: In this study, we were able to document absence of a relationship between progression of disease in skin or lymph nodes and C-KIT expression. Neither there was an association between large cell transformation and expression of CD117.Most of the positive cells appear to be mast cells. These findings are in contrast to previous reports of presence of CK 117 in CTCLs specially with CD 30 cells and in concert with recent paper by Medeiros et al –which contributes previous reports to use of oversensitive anibody. We are in process of performing PCR to confirm our findings.

187 STROMAL INVASION AND NODAL METASTASIS IN EXTRAMAMMARY PAGET'S DISEASES
Yasuka Miyakuni; Toshiharu Matsumoto; Yuki Yamada; Astushi Arakawa; Hiroshi Sonoue; Koichi Suda, Juntendo University School of Medicine, Tokyo, Japan
Background: In extramammary Paget's disease (EMPD), stromal invasion and nodal metastasis are occasionally seen. However, a detailed study focusing these phenomena has not been published. Thus, the purpose of the present study is to clarify stromal invasion and nodal metastasis in EMPD.
Design: The examined cases consisted of 35 cases, in which wide resection was performed. The examined materials, consisted of scrotum, penis and inguinal lesion from 27 males, and vulva from 8 females. Sections for histological study were obtained from resected materials, and histological sections were stained with conventional stains.
Results: Stromal invasion was found in 16 cases (46%); superficial stromal invasion in 12 cases and deep stromal invasion in 4 cases. In 15 cases, inguinal lymph nodes were dissected, and nodal metastasis was noted in 5 cases. Nodal metastasis with or without stromal invasion group consisted of 0% (0/9) in non-invasion group, 80% (4/5) in mild invasion group and 100% (1/1) in severe invasion group.
Conclusion: In EMPD, stromal invasion is a frequent event, and patients with stromal invasion relates to nodal metastasis.

188 QUANTITATIVE ANALYSIS OF CCL21, CCL19, AND CCR7 MRNA EXPRESSION IN PRIMARY AND METASTATIC CUTANEOUS MALIGNANT MELANOMA
Carlos Monteagudo; David Ramos, University of Valencia, Valencia, Spain; *Vicent Alonso*, Hospital Clinico Universitario, Valencia, Spain; *José Antonio López-Guerrero*, Fundacion Instituto Valenciano de Oncologia, Valencia, Spain; *Esperanza Jorda*, Hospital Clinico Universitario, Valencia, Spain; *Antonio Llombart-Bosch; Antonio Pellin*, University of Valencia, Valencia, Spain
Background: A role for the CCR7 chemokine receptor in melanoma lymph node metastasis has been proposed. The fact that CCR7 ligands, CCL21 and CCL19, are expressed in lymph node and lymphatic vessels supports the hypothesis that a gradient concentration of these chemokines might facilitate lymph node metastasis.
Design: Our goal was to quantify mRNA expression of CCR7 and its ligands, CCL21 and CCL19, in primary and metastatic human cutaneous malignant melanomas in order to determine if there is a gradient expression of both chemokines between primary and metastatic lesions which could be responsible for the metastatic dissemination of human melanoma. CCR7, CCL21 and CCL19 mRNA expression was evaluated by Real-Time Quantitative PCR in 62 frozen tissue samples from primary and metastatic melanoma: <=1 mm, (n=15), >1mm (n=15), "in transit" metastases(n=14), lymph node metastases (n=10), and distant metastases (n=8). In order to evaluate the cell types responsible for chemokine ligand and receptor expression, an immunohistochemical study (avidin-biotin immunoperoxidase technique) was also performed in adjacent frozen sections.
Results: CCL21 and CCL19 mRNA levels were significantly higher in thin primary melanomas than in thick tumors (p=0,019; p=0,016), in transit metastases (p=0,000, p=0,000), lymph node metastases (p=0,007, p=0,016) , and distant metastases (p=0,000, p=0,000). CCR7 mRNA levels were also higher in thin tumors than in "in transit" and lymph node metastases (p=0,022). CCL21 and CCL19 immunoreactivity was found in endothelial cells of lymphatic vessels and high endothelial venules of lymph nodes as well as in some tumor cells. CCR7 immunostaining was present in dendritic and tumor cells in primary and metastatic lesions.
Conclusion: The fact that the highest CCL21 and CCL19 chemokine levels are present in thin primary melanomas suggests that these chemokine ligands might retain CCR7+ tumor cells in the primary site in these patients. In contrast, the lower levels of both chemokines in thick melanomas support its potential implication in lymph node metastasis of CCR7+ tumor cells. *Performed with FIS-PI030512 grant, from Fondo de Investigación Sanitaria, Spain.

189 UPREGULATION OF TELOMERE-INDEPENDENT APOPTOSIS CHARACTERIZES CUTANEOUS MALIGNANCIES IN OLDER PATIENTS
Jane Moorhead; Salvador J. Diaz-Cano, King`s College Hospital, London, United Kingdom
Background: There are controversial results on the influence of age on malignancy prognosis, being the patient age used as staging criteria (e.g., thyroid neoplasms). To test biologic features that can explain differences in tumors by age, the skin model was selected for two main reasons: tumors tend to be detected relatively early due to their easy access and a whole variety of common neoplasms (carcinomas, melanomas, sarcomas and lymphomas) can be analyzed.
Design: We selected 50 cases of nodular basal cell carcinomas, well-differentiated squamous cell carcinoma, superficial spreading malignant melanoma, dermatofibrosarcoma protuberans, and patch stage mycosis fungoides that have appropriate archival material. Representative samples were evaluated by standard immunohistochemistry for Ki67, telomerase, mlh1, msh2, In situ end labeling of DNA fragments (TUNNEL for apoptosis detection), and FISH-PNA of telomere. The tests were assessed in the whole lesion and the positive cells expressed as percentage of tumor cells. Appropriate controls were run in each sample. Cases were stratified according to patient's age in <50 years (group A, 10 cases), 50-70 years (group B, 30 cases) and >70 years (group C, 10 cases). The results were statistically compared using analysis of variance and Student t-test, and considered significant if $P<0.05$.
Results: The average age in each group was 34 (group A), 59 (group B) and 78 years (group C). All neoplasms were revealed positive for mlh1 and msh2, regardless of the age group. Proliferation and the percentage of FISH-detectable telomere revealed and inverse correlation, being proliferation significantly higher in group A than in group C; telomere revealed the opposite pattern. Apoptosis and the global kinetic index Ki67×Telomere/TUNNEL (%) were significantly higher in group C as compared with A and B ($P=0.0003$ and $P=0.0006$). Group B was heterogeneous, cases being able to stratified by group A and C patterns.
Group A/ Group B/ Group C
<50/ 50-70/ >70
Ki67/ 19.74/ 16.75/ 15.40
Telomere FISH/ 41.66/ 53.97/ 53.25
Ki67×Telomere (%)/ 3.42/ 7.35/ 7.56
TUNNEL / 0.50/ 2.82/ 10.17
Ki67×Telomere/TUNNEL (%) / 31.64/ 26.49/ 43.94
Conclusion: In the absence of mismatch repair abnormalities, malignancies in older patients are defined by significantly increased apoptosis, related with a telomere-independent accumulation of genetic alteration that is facilitated by lower cellular turnover.

190 ECCRINE SYRINGOFIBROADENOMA OF THE SKIN. CASE REPORT AND LITERATURE REVIEW
Danilo Odashiro, LAC-Laboratorio, Ocular Pathology Laboratory McGill, Ophthalmology UNIFESP, Campo Grande, Brazil; *Jeferson Cavalcante*, Hospital do Cancer, Campo Grande, Brazil; *Luciana Miiji; Macanori Odashiro; Neuza Odashiro; Cristina Katayama; Patricia Pereira,* LAC-Laboratorio de Anatomia Patologica e Citopatologia, Campo Grande, Brazil; *Alexandre Odashiro*, Lac-Laboratorio, Ocular Pathology McGill, University for Pantanal Region and State Development, Campo Grande, Brazil
Background: Eccrine syringofibroadenoma (ES) is a rare benign neoplasm arising from the intraepidermal portion of eccrine ducts. There are approximately 60 cases of ES reported in the English literature, and in recent years the lesion has been described as occurring in association with other skin conditions.
Design: To report one case of ES on the face.
Result: A 71 year-old male complained of a lesion on his left cheek that had been presented for 5 years with occasional bleeding without major changes. Physical examination revealed a 1,5 cm well-delimitated reddish lesion on his left cheek. A few seborrheic keratosis were also present. The clinical differential diagnosis included Dermatofibroma and Hemangioma. The lesion was totally excised with free margins. The microscopic exam showed a tumor with thin anastomosing epithelial cords and strands forming a net and connected to the undersurface of the epidermis. The cells were smaller and more basophilic than the epidermal keratinocytes. The epithelial strands showed ductal differentiation, often associated with a well-formed cuticle. Between the strands there was a rich fibrovascular stroma with adipocytes. No cellular atypia was present. The diagnosis of ES was made.
Conclusion: We presented a case of a rare benign eccrine tumor with approximately 60 cases reported in the English literature to date.

191 ISOFORM-SPECIFIC REGULATION OF THE ACTIN-ORGANIZING PROTEIN PALLADIN DURING TGF-β1-INDUCED MYOFIBROBLAST DIFFERENTIATION
Mikko Rönty, University of Helsinki, Helsinki, Finland; *Suvi-Katri Leivonen*, University of Turku, Turku, Finland; *Boris Hinz*, Swiss Federal Institute of Technology, Lausanne, Switzerland; *Andrew Rachlin; Carol Otey,* University of North Carolina, Chapel Hill, NC, United States; *Veli-Matti Kähäri; Olli Carpen*, University of Turku, Turku, Finland
Background: Contractile myofibroblasts are responsible for remodeling of extracellular matrix during wound healing. However, their continued activity results in various fibrocontractive diseases. Conversion of fibroblasts into myofibroblasts is induced by transforming growth factor-β1 (TGF-β1) and is hallmarked by the neo-expression of α-smooth muscle actin (SMA), a commonly used myofibroblast marker. Moreover, myofibroblast differentiation and acquisition of the contractile phenotype involves functionally important alterations in the expression of actin-organizing proteins. Palladin is a recently identified cytoskeletal protein that controls the integrity of actin-containing stress fibers. It is expressed as several isoforms, including major 3Ig (90 kDa) and 4Ig (140 kDa) forms that differ in their N-terminal sequence.
Design: Our purpose was to investigate, using cultured fibroblasts, a rat skin wound model and human tissue specimens, (1) whether myofibroblast differentiation is accompanied by changes in the expression of palladin, and (2) which signaling pathways regulate expression of palladin.
Results: Cultured untreated fibroblast express only palladin 3Ig isoform. However, TGF-β1 induces neoexpression of palladin 4Ig isoform within 24 h. The expression of palladin precedes upregulation of SMA, which is upregulated only after 48 h. Palladin was located to the dense regions of robust actin stress fibers and to focal adhesions. Elucidation of the TGF-β1 signaling pathways showed that Smad signaling, in particular via Smad3, mediates the TGF-β1-induced upregulation of palladin and SMA in fibroblasts. Further studies implied additional role for ERK1/2 and p38 pathways in regulating palladin gene expression. Analysis of the rat skin wound model showed that palladin 4Ig isoform is not expressed in fibroblasts of early (3d) wound granulation tissue that do not exhibit microfilament bundles. However, day 6 post-wounding granulation tissue fibroblasts de novo express palladin 4Ig isoform in conjunction with the development of stress fibers (i.e. acquisition of the proto-myofibroblast phenotype). Thus, palladin expression

Upregulation of telomerase-independent apoptosis characterizes cutaneous malignancies in older patients

Moorhead J, Diaz-Cano SJ

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Background:

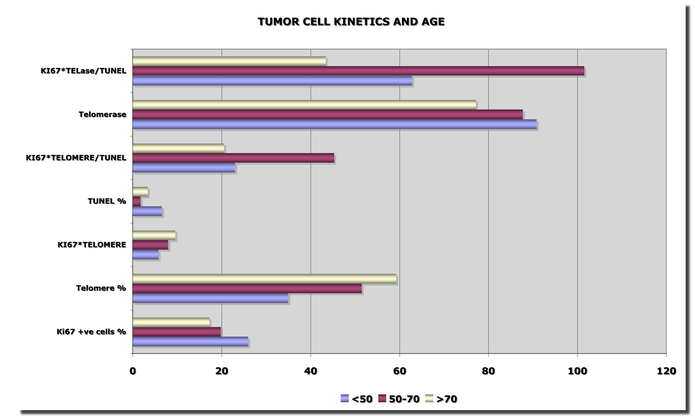
There are controversial results on the influence of age on malignancy prognosis, being the patient age used as staging criteria (e.g., thyroid neoplasms). To test biologic features that can explain differences in tumors by age, the skin model was selected for two main reasons: tumors tend to be detected relatively early due to their easy access and a whole variety of common neoplasms (carcinomas, melanomas, sarcomas and lymphomas) can be analyzed.

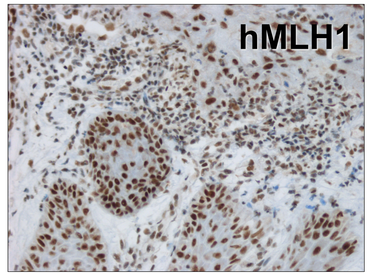
Design:

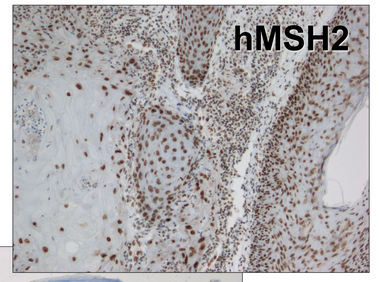
We selected 50 cases of nodular basal cell carcinomas, well-differentiated squamous cell carcinoma, superficial spreading malignant melanoma, dermatofibrosarcoma protuberans, and patch stage mycosis fungoides that have appropriate archival material. Representative samples were evaluated by standard immunohistochemistry for Ki67, telomerase, mlh1, msh2, In situ end labeling of DNA fragments (TUNNEL for apoptosis detection), and PNA-FISH of telomere. The tests were assessed in the whole lesion and the positive cells expressed as percentage of tumor cells. Appropriate controls were run in each sample. Cases were stratified according to patient's age in ≤50 years (group A, 10 cases), 50-70 years (group B, 30 cases) and >70 years (group C, 10 cases). The results were statistically compared using analysis of variance and Student *t*-test, and considered significant if P<0.05

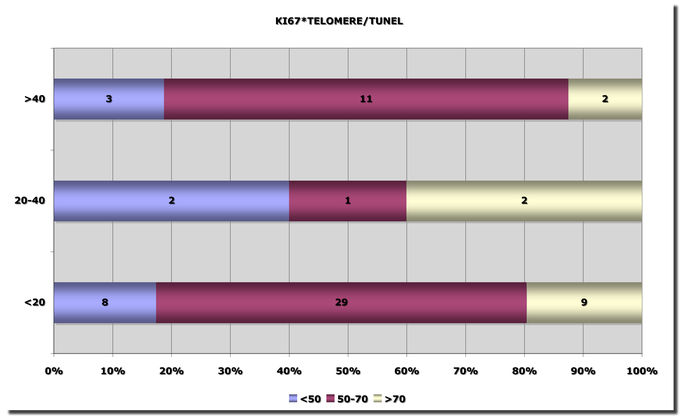
Results:

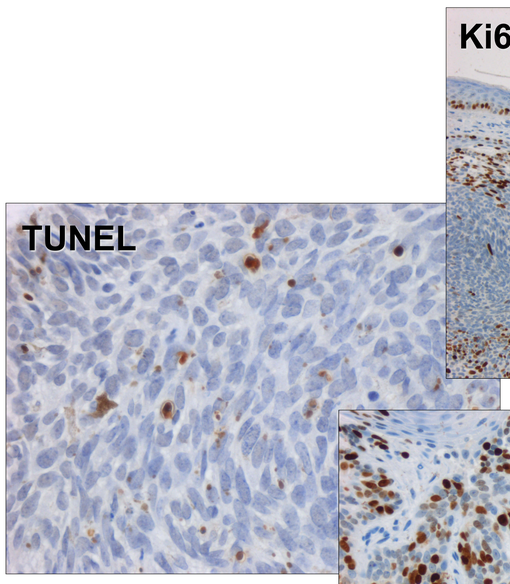
The average age in each group was 34 (group A), 59 (group B) and 78 years (group C). All neoplasms were revealed positive for mlh1 and msh2, regardless of the age group. Proliferation and the percentage of FISH-detectable telomere revealed and inverse correlation, being proliferation significantly higher in group A than in group C; telomere revealed the opposite pattern. The global kinetic index Ki67×Telomere/TUNNEL (%) were significantly higher in group B as compared with A and C (P=0.0003 and P=0.0006), due to apoptosis down-regulation.

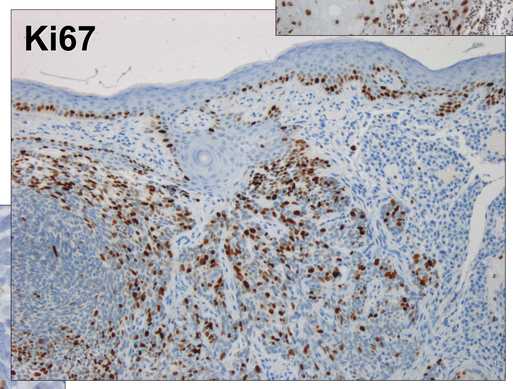


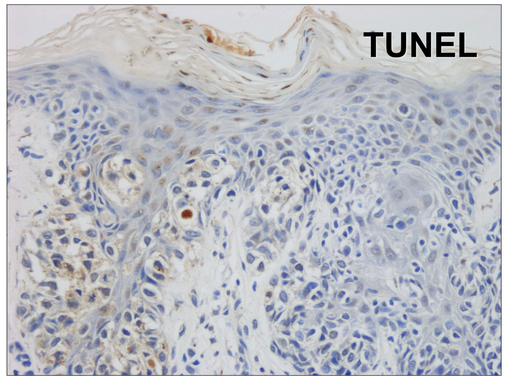


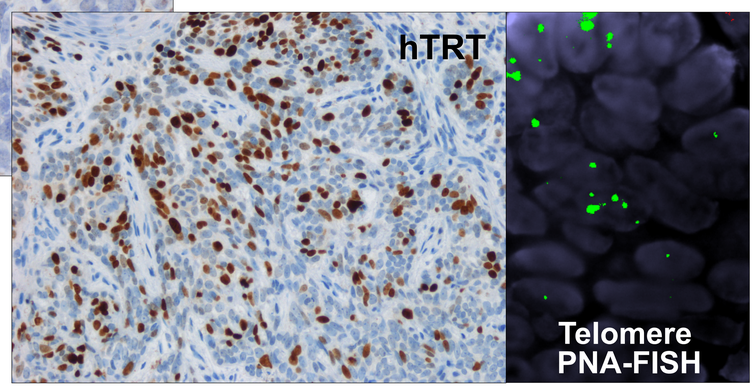


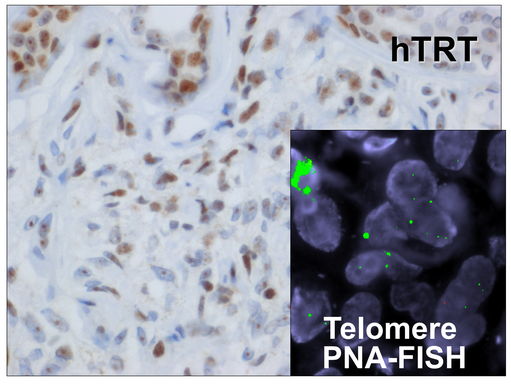












Conclusions:

In the absence of mismatch repair abnormalities, malignancies in middle aged patients are defined by significant apoptosis down-regulation and a lower cellular turnover both facilitating a telomere-independent accumulation of genetic alterations.

* = Statistically significant differences