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1. Green AC, McBride P.
Clin Evid (Online). 2014 Aug 18;2014. pii: 1709.
PMID: 25137222 [PubMed - as supplied by publisher]

☐ [Locally advanced and unresectable cutaneous squamous cell carcinoma: outcomes of concurrent cetuximab and radiotherapy.](#)

2. Samstein RM, Ho AL, Lee NY, Barker CA.
J Skin Cancer. 2014;2014:284582. doi: 10.1155/2014/284582. Epub 2014 Jul 21.
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☐ [Non-Structural protein 1 \(NS1\) gene of Canine Parvovirus-2 regresses chemically induced skin tumors in Wistar rats.](#)

3. Santra L, Rajmani RS, Ravi Kumar GV, Saxena S, Dhara SK, Kumar A, Sahoo AP, Singh LV, Desai GS, Chaturvedi U, Kumar S, Tiwari AK.
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Skuamöz hücreli karsinoma
gelişimi önlenabilir mi?



Epidemiology and risk factors for cutaneous squamous cell carcinoma

Topic Outline

SUMMARY ➔

INTRODUCTION

EPIDEMIOLOGY

- Geographic variation
- Age
- Ethnicity

RISK FACTORS

- UV light exposure
 - UVB radiation
 - UVA radiation
- Ionizing radiation
- Immunosuppression
- Chronic inflammation
- Arsenic exposure
- Genetic alterations
- Family history
- Inherited disorders
 - Xeroderma pigmentosum
 - Epidermolysis bullosa
 - Albinism
- Epidermodysplasia verruciformis
 - Other genetic syndromes
- Smoking
- Diet

Epidemiology and risk factors for cutaneous squamous cell carcinoma**Authors**

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Robert S Stern, MD
June K Robinson, MD

Disclosures: Jean Lee Lim, MD Nothing to disclose. Maryam Asgari, MD, MPH Nothing to disclose. Robert S Stern, MD Conflicts of interest related to Squibb [Skin reactions (Drug no longer under development for hepatitis C, diabetes drugs)]. Other Financial Interest: Law firms [Corbin & McNeil and Eisei (Ibuprofen, Alzheimer drugs)]. June K Robinson, MD Nothing to disclose. Rosamaria Corona, MD, DSc Employment by Squibb.

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Literature review current through: Jun 2014. | **This topic last updated:** Mar 17, 2014.

INTRODUCTION — Cutaneous squamous cell carcinoma (SCC) is a common cancer arising from malignant transformation of keratinocytes. The development of SCC is dependent upon exposure to risk factors (most importantly ultraviolet light) and patient-specific factors.

The epidemiology and risk factors of cutaneous SCC will be reviewed here. The clinical features, diagnosis, treatment, and prognosis of cutaneous SCC are discussed elsewhere. (See "[Clinical features and diagnosis of cutaneous squamous cell carcinoma \(SCC\)](#)" and "[Evaluation and management of cutaneous squamous cell and basal cell carcinoma](#)" and "[Treatment and prognosis of cutaneous squamous cell carcinoma](#)".)

EPIDEMIOLOGY — Cutaneous squamous cell carcinoma (SCC) is the second most common type of skin cancer (after basal cell carcinoma [BCC]), and accounts for approximately 20 percent of nonmelanoma skin cancers [1-3]. Because cutaneous SCC is a highly heterogeneous malignancy, the exact incidence of this malignancy is unknown.

Epidemiologic studies often combine data on SCC, BCC, and other nonmelanocytic skin tumors. Such studies have reported that the highest incidence rates reported in the United States is from a population-based study that utilized government office visits to estimate the number of new skin cancer diagnoses in the United States [4]. The authors estimated that approximately 1.3 million new cases of BCC, SCC, and other less common nonmelanoma skin cancers occurred in 2006. (See "[Epidemiology and risk factors for cutaneous squamous cell carcinoma](#)".)

Üzüm çekirdeđi ekstresi

415 SCC 'li ve kontrol grubunda yapılan alıřmada, üzüm çekirdeđi ekstresinin SCC oluřum riskini azalttıđı gösterilmiř

Siyah ay

Daha önceleri siyah ayda bulunan D-limonene tüketiminin SCC oluřum riskini azalttıđı bildirilse de son yapılan alıřmada bu desteklenmemiř

NSAID

Hayvan çalışmalarında NSAID'lerin SCC gelişimini önleyebileceği bildirilse de insan kaynaklı çalışmalarda bu desteklenmemiştir

Topikal tretinoinin

- 1131 hastalık geniş seri, çok merkezli, randomize çalışmada
- Topikal tretinoinin SCC gelişimini önlemediği gösterilmiş

The relevance of the vitamin D endocrine system (VDES) for tumorigenesis, prevention, and treatment of non-melanoma skin cancer (NMSC)

Present concepts and future perspectives

Jörg Reichrath* and Sandra Reichrath

Klinik für Dermatologie, Venerologie und Allergologie; Universitätsklinikum des Saarlandes; Homburg/Saar, Germany

The data presented in this review provide convincing evidence that the VDES is of high importance for prevention (Tables 1 and 2) and treatment of NMSC. Besides a sufficient vitamin D status, the molecular basis that underlies these preventive

Vitamin D endokrin sistem

- Vitamin D reseptörleri derideki bir çok hücrede bulunmakta
- Değişik epidemiyolojik ve invitro çalışmalar vitamin D ve metabolitlerinin SCC oluşumunu azalttığını göstermiş
- Bu etkisini p53 bağımlı DNA hasarını değiştirmekle oluşturmakta
- D vitamini UV etkisi ile deride üretilmekte
- Bu sonuç UV'nin SCC oluşumunda hem faydalı hem de zararlı etkileri olduğunu ortaya koymakta
- Bu konudaki yeni yapılacak çalışmalar ileride SCC tedavisinde D vitaminin yerini ortaya koyacaktır

Omega 3 yağ asitleri

- Yapılan bir çok invivo çalışma omega 3 yağ asitlerinden zengin beslenmenin deri kanserlerinden koruyucu olduğunu ileri sürmüştür



Consumption of omega-3 fatty acids and the risk of skin cancers: A systematic review and meta-analysis

Sophie E. Noel¹, Adam C.S. Stoneham², Catherine M. Olsen³, Lesley E. Rhodes^{4,5} and Adele C. Green^{3,4,5}

¹Albany Health Campus, Warden Avenue, Albany, WA, Australia

²Department of Oncology, Churchill Hospital, Oxford, United Kingdom

³Queensland Institute of Medical Research, Royal Brisbane Hospital, QLD, Australia

⁴Dermatology Centre, Institute of Inflammation and Repair, Faculty of Medical and Human Sciences, University of Manchester, Manchester, United Kingdom

⁵Salford Royal NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom

available (OR 0.52, 95% CI 0.34–0.78), and SCC, although nonsignificantly (pooled OR 0.86, 95% CIs 0.59–1.23). Available evidence is suggestive, but currently inadequate, to support the hypothesis that n-3 PUFAs protect against skin malignancy.

- Bu alanda yapılmış güvenlik derecesi yüksek çalışmaları inceleyen meta analitik bir çalışma
- Bu konuda destekleyici sonuçlar olsa da henüz yeterli bilgi yoktur

Skvamöz hücreli kanser etyolojisinde gelişmeler



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- 1380 psoriasisli hasta, 30 yıllık prospektif, kohort çalışma
- 450 seanstan fazla PUVA alanlarda SCC gelişim riski 35 kat fazla

- Bir kemateropetik olan serofenibe bağlı RAF inhibisyonu sonucu
- CDKN2A lokusu ve RAS yolağı mutasyonunun SCC ile ilişkili olduğu gösterilmiş

- Ailede SCC hikayesinin olması hastalığın gelişimi için artmış risk oluşturmakta
- [Kharazmi E, Fallah M, Sundquist K, Hemminki K. Familial risk of early and late onset cancer: nationwide prospective cohort study. BMJ 2012; 345:e8076.](#)

- Metaanalitik çalışma
- Solaryum alanlarda almayanlara göre % 67 oranında SCC oluşma riski var
- [Wehner MR, Shive ML, Chren MM, et al. Indoor tanning and non-melanoma skin cancer: systematic review and meta-analysis. BMJ 2012; 345:e5909.](#)

- Geniş metaanalitik, olgu kontrollü derleme
- Sigara içme SCC için risk faktörü, fakat etyolojik ajan olduğuna karar vermek için yeni çalışmalara ihtiyaç var
- [Leonardi-Bee J, Ellison T, Bath-Hextall F. Smoking and the risk of nonmelanoma skin cancer: systematic review and meta-analysis. Arch Dermatol 2012; 148:939.](#)

- Fotosensitif ilaçların SCC oluşum riskini artırdığı gösterilmiş
- [Goyal RK, Gehris RP, Howrie D, et al. Phototoxic dermatoses in pediatric BMT patients receiving voriconazole. Pediatr Blood Cancer 2014; 61:1325.](#)
- [Robinson SN, Zens MS, Perry AE, et al. Photosensitizing agents and the risk of non-melanoma skin cancer: a population-based case-control study. J Invest Dermatol 2013; 133:1950.](#)

J Cutan Med Surg. 2013 Mar-Apr;17(2):139-42.

Squamous cell carcinoma developing after CO2 laser resurfacing.

Nicoli F¹, Balzani A, Gentile P, Lazzeri D, Di Pasquali C, Nicoli M, Bocchini I, Cervelli V.

⊕ Author information

Abstract

BACKGROUND: Skin resurfacing with the carbon dioxide (CO₂) laser is currently a popular means of improving rhytides and scars and has been reported useful in the treatment for photodamaged skin, including precancerous and benign skin lesions, as well as superficial benign pigmented lesions.

- CO2 lazer deri yenilemede kullanılan popüler bir tedavi yöntemidir
- 68 yaşında erkek hastada CO2 lazer yaptırdıktan 3 hafta sonra uygulama bölgesinde SCC gelişmiş

ORIGINAL ARTICLE

Risk of subsequent cutaneous squamous cell carcinoma in patients with melanoma

Maryam M. Asgari, MD, MPH,^{a,b} E. Margaret Warton, MPH,^a Charles P. Quesenberry, PhD,^a
Daniel O. Koralek, PhD,^c and Michael Taylor, PhD^c
Oakland and San Francisco, California

- 5 yıllık süre ile MM'lu hastalar takip edilmiş
- Hastaların % 12'sinde SCC ortaya çıkmış
- Bu hastaların çoğunluğu 60 yaşın üstünde, erkek ve daha önce non melanoma deri kanseri geçirme hikayesi olan veya öncü bir kanseri olan kişiler

Role of human papillomavirus in cutaneous squamous cell carcinoma: A meta-analysis

Jennifer Wang, BA,^a Bishr Aldabagh, MD,^b Justin Yu, BS,^c and Sarah Tuttleton Arron, MD, PhD^b
Valballa, New York; San Francisco, California; and St Louis, Missouri

Conclusion: These results contribute to evidence that HPV is associated with cuSCC. Higher HPV burden in tumors from immunosuppressed patients compared with immunocompetent patients may have therapeutic implications. (J Am Acad Dermatol 2014;70:621-9.)

- HPV SCC ilişkisi ile ilgili bir çok çalışma yapılmış ve farklı sonuçlar elde edilmiştir
- Güvenilir derecesi yüksek çalışmaları inceleyen meta analitik makale
- Hem immün süpresif hem de normal kişilerde SCC'li dokuda normal dokuya göre istatistiki olarak anlamlı derecede HPV yükü tespit edilmiş
- Bu sonuç tümör yükünü azaltmak ve daha iyi tedavi sonuçları elde etmek adına hedefe yönelik yeni tedavi seçenekleri için yol gösterici olabilir

Urinary Melatonin Levels and Skin Malignancy

Reza Ghaderi¹, MD; Samineh Sehatbakhsh², MD; Mehdi Bakhshaei², MD; Gholam Reza Sharifzadeh³, MSc

Abstract

Melatonin inhibits tumor genesis in a variety of in vivo and in vitro experimental models of neoplasia. In industrialized societies, light at night, by suppressing melatonin production, poses a new risk for the development of a variety of cancers such as breast cancer. This effect on skin has been previously studied only in animals and not in humans. Our goal was to examine the relationship between 24-hour 6-sulphatoxymelatonin levels and skin cancer in a case-control study of 70 patients with skin cancer and 70 healthy

Discussion

The results of the present study demonstrated that the case group had a lower level of 24-hour urinary 6-sulfatoxymelatonin, which may be interpreted that lower levels of melatonin are correlated with a rise in the risk of SCC and BCC. Our results chime in

Melatonin ve SCC

- İnvivo ve invitro bir çok kanser çalışmasında melatoninin tümör oluşumunu inhibe ettiği gösterilmiştir
- Gece ışıklandırmanın giderek artmasıyla melatonin üretiminin baskılanması bu riski de artırmaktadır
- Deri kanserlerindeki melatonin etkisini gösteren ilk çalışma

Melatonin ve SCC

- SCC'li hastalarda 24 saatlik idrarda melatonin metabolitinin (6-sulphatoxymelatonin) sağlıklı kontrollere göre düşük olduğu bulunmuş
- Melatonin ve düzenli gece uykusunun deri kanserinin önlenmesinde yardımcı bir faktör olabileceği ileri sürülmüş

ARTICLE

Nonmelanoma Skin Cancer After Kidney Transplant

Merih Tepeoğlu,¹ Şebnem Ayva,¹ Alev Ok Atılgan,¹ M. Zeyneb Tunca,¹ B. Handan Özdemir,¹ Gökhan Moray,²
Sedat Yıldırım,² Gülnaz Arslan,³ Mehmet Haberal²

- Böbrek nakli yapılan hastalarda SCC görülme oranı yüksek
- 1275 böbrek nakli yapılan hastanın 33 (%2.4)'ünde NMDK gözlenmiş
- Bu hastaların %30'u SCC
- Böbrek nakli yapılan hastaların bu açıdan bilgilendirilmesi, UV'den korunmaları ve dermatolojik takibi önemli

REVIEW ARTICLE

Risk of cancer in psoriasis: a systematic review and meta-analysis of epidemiological studies

C. Poupard,¹ E. Brenaut,² C. Horreau,³ T. Barnetche,⁴ L. Misery,² M.-A. Richard,³ S. Aractingi,⁵ F. Aubin,⁶ B. Cribier,⁷ P. Joly,⁸ D. Jullien,⁹ M. Le Maître,¹⁰ J.-P. Ortonne,¹¹ C. Paul^{1,*}

- Psoriasis ve kanser riski artışı arasındaki ilişki tartışmalı bir konu
- Bu alanda yapılmış çalışmalardan derlenen geniş meta analitik bir makale
- Psoriasislilerde SCC riski artmış
- Bu artmış risk özellikle daha önceden alınan PUVA tedavisi, siklosporin ve metotreksat tedavisine bağlı olarak görülmekte

Moleküler çalışmalar ve tümör genetiği

SCC progresyon belirteci

- SCC progresyonunu belirleyen bir çok moleküler belirteç tanımlanmış
- Fakat şu ana kadar klinik pratikte kullanılabilecek bir belirteç henüz yoktur

Squamous cell carcinoma of the skin: Emerging need for novel biomarkers

Atte Kivisaari, Veli-Matti Kähäri

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Atte Kivisaari, Veli-Matti Kähäri, MediCity Research Laboratory, University of Turku, FI-20521 Turku, Finland

Author contributions: Kivisaari A and Kähäri VM contributed to the writing of this manuscript.

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sion of cSCC have been identified.

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Key words: Squamous cell carcinoma; Skin cancer; Biomarker; Matrix metalloproteinase; Serpin

Core tip: Several molecular markers for progression of cutaneous squamous cell carcinoma (cSCC) have been identified, but a clinically useful panel of biomarkers is still not available. Further studies are required to determine whether prognostic cSCC biomarker panel can be incorporated into clinical practice. In the meantime, while waiting for novel diagnostic and prognostic tools.

Matriks metalloproteinaz-7

- Matriks metalloproteinaz-7 (MMP7) derideki ekstrasellüler matriks preteolizinde rol alan bir moleküdür
- MMP7 ekspresyonun özellikle agresiv SCC başta olmak üzere SCC'li dokuda arttığı gösterilmiş
- MMP7'nin baskılanması ile SCC'de büyüyen tümör hücrelerinin baskılandığı görülmüş
- Agresiv SCC'de hedefe yönelik tedavi açısından önemli olabilir

Serin peptidaz inhibitörleri(Serpinler)

- Serpinler peptidaz inhibitörü olarak görev yaparlar
- SCC'li dokuda SerpinA1'in arttığı ve bunun tümör progresyonu ile korele olduğu tespit edilmiş
- SerpinA1 SCC'de prognostik bir biomarker olarak kullanılabilir

 Minireview

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Conflict of interest

None.

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New developments in dermatological oncogenetics

Molecular tumorigenesis of the skin

Yoshiaki Kubo¹, Yoshihiro Matsudate¹, Nozomi Fukui¹, Ayaka Nakasuka¹,
Maiko Sogawa¹, Mika Oshima¹, Tomoya Mizutani¹, Masanobu Otsu¹,
Kazutoshi Murao¹, and Ichiro Hashimoto²

¹Department of Dermatology, ²Department of Plastic and Reconstructive Surgery, Institute of Health Biosciences, the University of Tokushima Graduate School, Tokushima, Japan

J. Med. Invest. 61 : 7-14, February, 2014

- Onkogenler ve tümör süpresör genlerde oluşan mutasyona bağlı intersellüler sinyal yollarının aktivasyonu farklı malin tümörlerin oluşumunda önemli rol oynamakta
- Bu sinyal yollarının belirlenmesi ile bunlara uygun hedefe yönelik tedavi ajanları ortaya konulabilecektir
- SCC'de NOTCH1/2 sinyal yolağında mutasyon son zamanlarda ortaya konmuştur

- NOTCH reseptörleri çeşitli hücre yüzeyinde bulunan protein yapısında, hücre farklılaşmasında düzenleyici rol alan moleküldür
- NOTCH1/2'nin tümör gelişiminde rolleri tam olarak bilinmese de deneysel çalışmalarda fare derisinde tümör süpresör olarak görev yapmakta

Yeni olgular

Squamous Cell Carcinoma of the Lip Associated With Adalimumab Therapy for Ankylosing Spondylitis: A Case Report and Review of TNF- α Inhibitors and Cutaneous Carcinoma Risk

Kristine B. Zitelli, MD; Daniel Zedek, MD; Prabha Ranganathan, MD; Erin Huiras Amerson, MD

- 29 yaşında bayan hasta, ankilozan spondiliti için 2 yıldır adalumimab kullanıyor
- Alt dudakta 3 haftadan beri oluşan 4 mm büyüklüğünde beyaz papül
- İnvaziv SCC



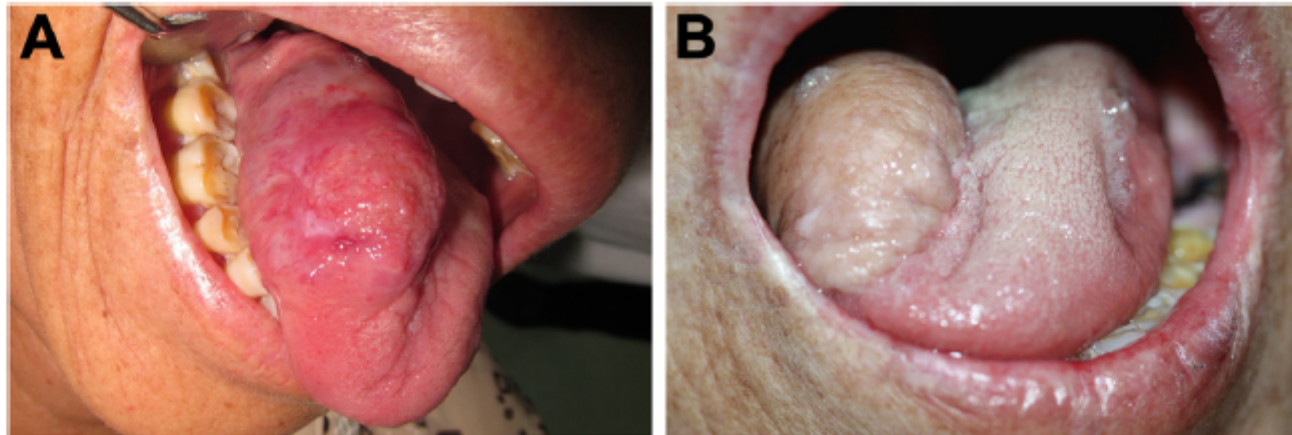
CASE REPORT

Open Access

Unexpected development of tongue squamous cell carcinoma after sclerotherapy for the venous malformation: a unique case report and literature review

Gang Chen^{1,2*†}, Xu Cai^{1†}, Jian-Gang Ren¹, Jun Jia^{1,2} and Yi-Fang Zhao^{1,2}

- 65 yaşında bayan hastada dildeki vasküler malformasyona intralezyonal skleroterapi ve rezeksiyon uygulanmış
- 5 yıl sonra dilde SCC gelişmiş
- Skleroterapi sonrası SCC gelişen ilk vaka



2 Clinical appearance. (A) Preoperative view of tumor showing a solid lesion with a cauliflower-like surface on the right side of the tongue. (B) Postoperative view of tongue at 6 months after hemiglossectomy and reconstruction with vascularized forearm flap.

Eruptive squamous cell carcinoma in a patient receiving abatacept for rheumatoid arthritis

To the Editor: Squamous cell carcinomas (SCCs) are common cutaneous malignancies, often arising from

- 45 yaşında bayan hasta
- Romatoid artriti, yaygın aktinik keratozları ve SCC lezyonları var
- RA için 3 yıl boyunca Abatacept kullanıyor
- Yeni bir SCC geliştiğinde Abatacept tedavisi kesiliyor
- Hastanın mevcut SCC lezyonları tedavi ediliyor ve izlemde yeni bir SCC lezyonu oluşmuyor
- RA hastasında Abatacepte bağlı SCC gelişen ilk vaka

Case Report

Squamous Cell Carcinoma Developing in a Cutaneous Lichen Planus Lesion: A Rare Case

- Kutanöz liken planusta malinite riskinin artmış olduğuna dair bir bilgi yok
- 36 yaşında erkek hastada 10 yıldır devam eden sol popliteal fossada hipertrofik liken üzerinde iyileşmeyen yara
- Histopatolojik incelemede verrüköz SCC



Tedavide
güncel

Features identified by the National Comprehensive Cancer Network as risk factors for recurrence of cutaneous squamous cell carcinoma

Location/size*
Poorly-defined borders
Recurrent tumors
Immunosuppressed patient
Site of previous radiation therapy or chronic inflammation
Rapidly growing tumor
Neurologic symptoms
Moderately or poorly differentiated tumor
Adenoid (acantholytic), adenosquamous, or desmoplastic subtypes
Depth ≥ 2 mm or Clark level IV or V
Perineural or vascular involvement

* Size ≥ 20 mm on trunk or extremities (excluding pretibia, hands, feet, nail units, and ankles); size ≥ 10 mm on cheeks, forehead, scalp, neck, or pretibia; size ≥ 6 mm on "mask areas" of the face (central face, eyelids, eyebrows, periorbital nose, lips [cutaneous and vermillion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear, genitalia, hands, and feet).

Source: Bichakjian CK, Alam M, Andersen J, et al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Basal Cell and Squamous Cell Skin Cancers, Version 1.2013. National Comprehensive Cancer Network, 2013.

CONCISE COMMUNICATION

Evaluation of sentinel node biopsy for cutaneous squamous cell carcinoma

Satoshi FUKUSHIMA,¹ Shinichi MASUGUCHI,¹ Toshikatsu IGATA,¹ Miho HARADA,¹ Jun AOI,¹ Azusa MIYASHITA,¹ Satoshi NAKAHARA,¹ Yuji INOUE,¹ Masatoshi JINNIN,¹ Shinya SHIRAISHI,² Yasuyuki YAMASHITA,² Tsuyoshi ISHIHARA,¹ Hironobu IHN¹

¹Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, and ²Department of Diagnostic Radiology, Kumamoto University, Kumamoto, Japan

- Sentinal lenf bezi biyopsisi SCC'de MM'daki gibi kabul edilmiş bir uygulama değildir
- Çalışma sonucunda SCC'de sentinal lenf bezi biyopsisi yapılmasının erken metastazları belirleme açısından önemli olduğu bildirilmiş



ELSEVIER



Guidelines for the excision of cutaneous squamous cell cancers in the United Kingdom: The best cut is the deepest

A.A. Khan^{a,*}, M. Potter^b, J.J. Cubitt^a, B.J. Khoda^d, J. Smith^c,
E.H. Wright^c, G. Scerri^d, A. Crick^c, O.C. Cassell^b, P.G. Budny^a

^a Department of Plastic Surgery, Stoke Mandeville Hospital, Aylesbury, United Kingdom

^b Department of Plastic Surgery, John Radcliffe Hospital, Oxford, United Kingdom

- SCC tedavisinde altın standart cerrahi eksizyon
- İngiliz Ulusal kanser rehberine göre düşük riskli tümörlerde 4 mm, yüksek riskli kanserlerde 6 mm radial sınırla eksizyonla %95 temizlenme
- İngilterede'ki 6 cerrahi merkezin 2 yıllık verileri retrospektif olarak incelenmiş
- Bu çalışmaya göre bu sınırların yetersiz olduğu gösterilmiş ve radial cerrahi sınırın daha derin olması gerektiği bildirilmiş



Non-melanoma skin cancers: Photodynamic therapy, cryotherapy, 5-fluorouracil, imiquimod, diclofenac, or what? Facts and controversies

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Fotodinamik tedavi

- PDT invaziv SCC'de tavsiye edilmez
- Yüzeyel SCC'de tedavi başarı oranı % 54
- SCC'de alternatif tedavi seçeneği
- Diğer seçenekler daha çok BCC'de

Conclusions

Surgical treatment of NMSC continues to be superior to non-surgical interventions. Perhaps, in time, topical therapies will gain further support and favor however, based on the current data, surgery remains the gold standard, save for the elderly or infirmed patient who is adverse to surgical intervention.

Hedefe yönelik tedaviler



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Review

Recent advances in head and neck squamous cell carcinoma – A review

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Anti-Tumour Treatment

Targeted therapies for squamous cell carcinoma of the head and neck:
Current knowledge and future directions

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- SSC'de Epidermal Growth Factor Receptor (EGFR) aktivitesi ve ekspresyonunda artış vardır
- SCC'de EGRF salınımını sağlayan signal yolları RAS/RAF/MEK/ERK, PI3-K/AKT, STAT yolağı, PLC/PKC, EGFR nükleer sinyal yolağı ve Src yolağı
- Cetuximab, panutumumab ve erlotinib gibi antikanser ilaçlar bu yolları baskılayarak etki göstermektedir

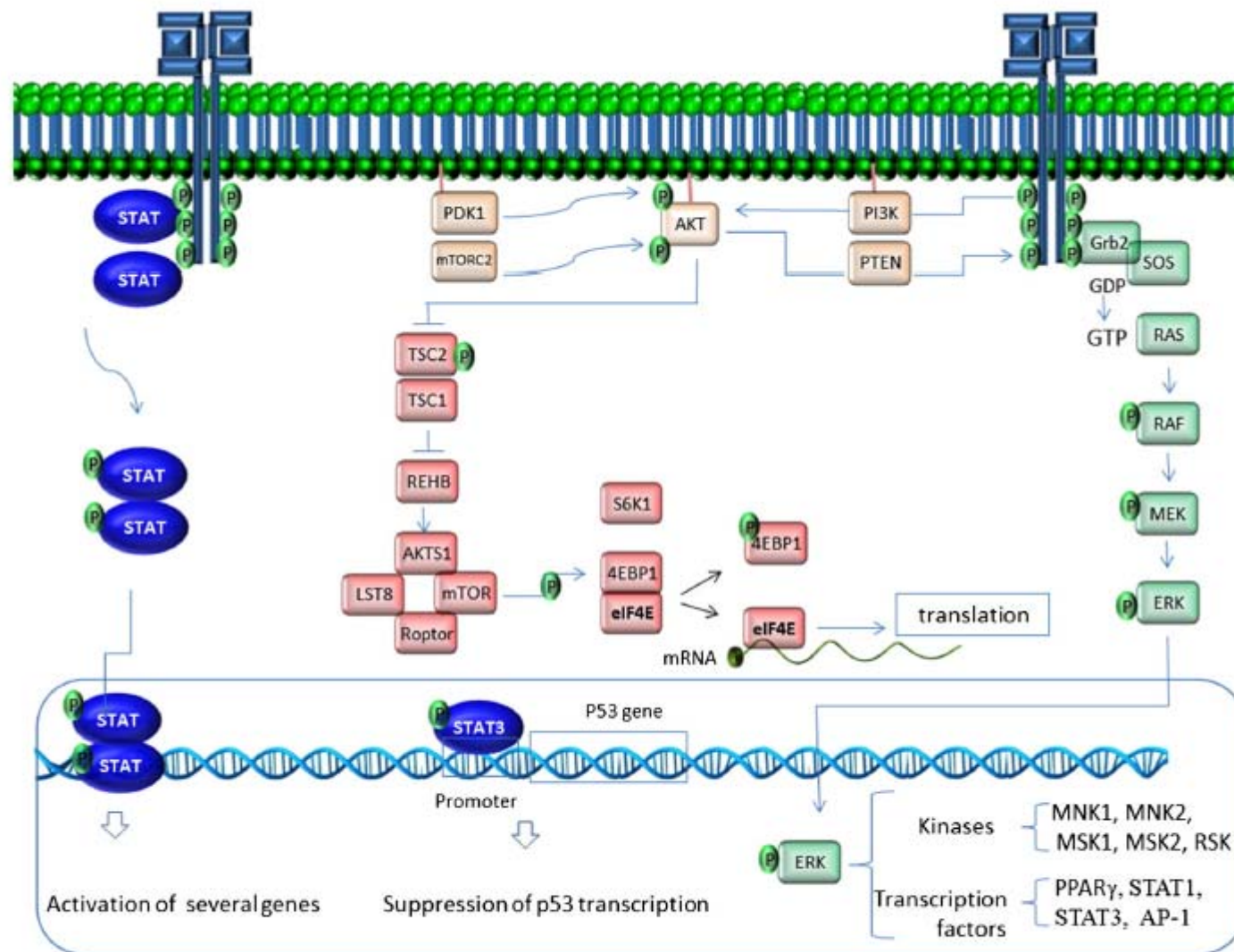


Fig. 1. RAF/RAS/MEK/ERK, PI3K/AKT and STAT pathways. Activation of RAF/RAS/MEK/ERK, PI3K/AKT finally leads to phosphorylation of several kinases and activation of a number of transcription factors. Upon activation of PI3K/AKT pathway, eIF4E is released and initiates the translation of some genes. This pathway is attenuated naturally by tumor suppressor PTEN, which dephosphorylates the AKT. After phosphorylation, STATs are dimerized and translocate into the nucleus, where they activate expression of several genes mostly involved in cell proliferation. STAT3 inhibits the transcription of p53 gene by occupying its promoter, indirectly resulting in enhanced cell proliferation.

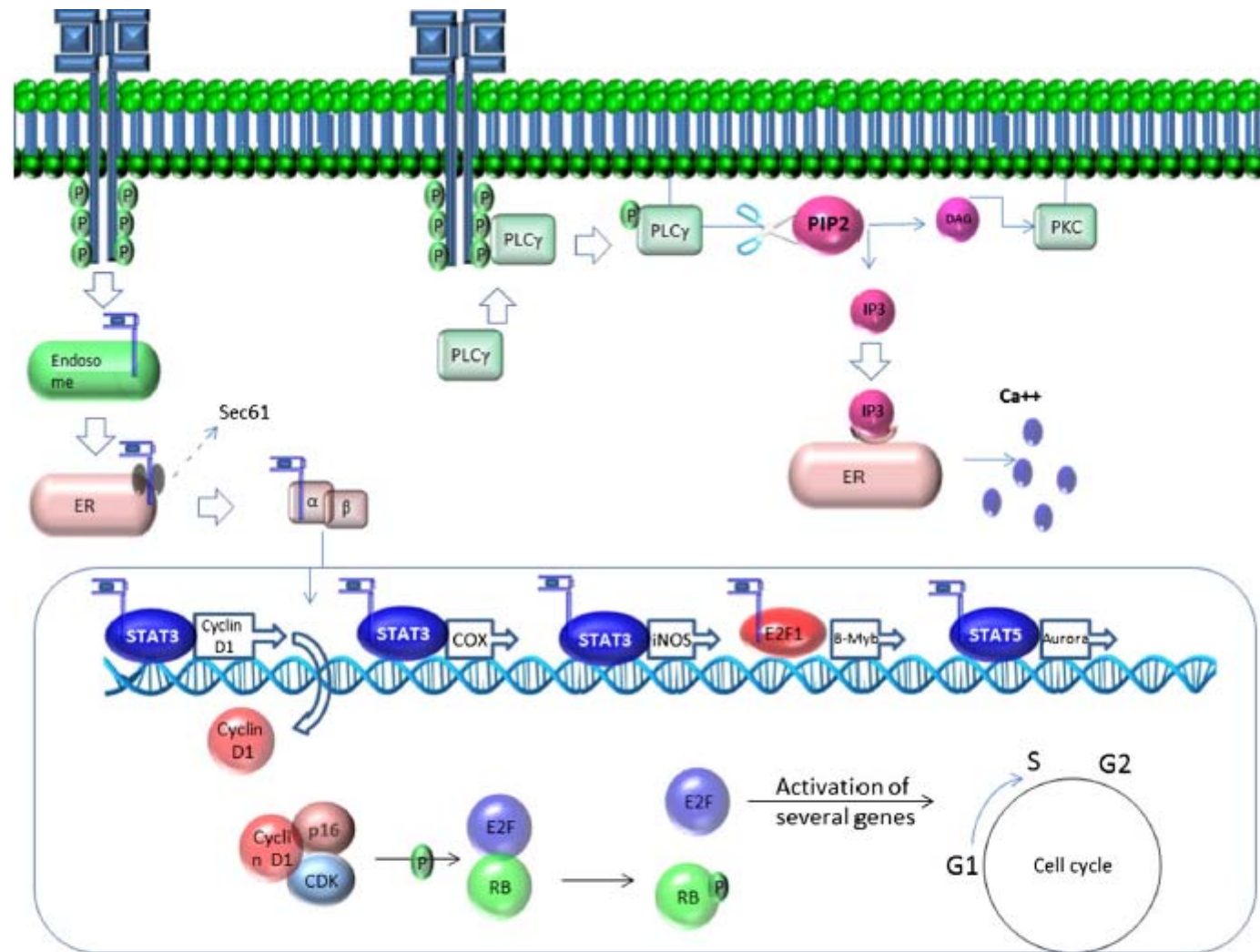


Fig. 2. PLCγ/PKC and EGFR nuclear signaling pathways. After being phosphorylated through the EGFR C-terminal, PLCγ binds to the cell membrane and cleaves PIP2 into diacylglycerol (DAG) and Phosphatidylinositol (3,4,5)-trisphosphate (IP3). IP3 binds to its specific receptor on the endoplasmic reticulum (ER) and induces calcium influx into the cell, and DAG activates the PLC through conformational change. Endosome, ER and importins mediate the translocation of EGFR from the cytoplasm into the nucleus, where it regulates (by mediation of STATs) the promoters of several target genes including cyclin D1, COX, iNOS, E2F1, B-Myb and aurora. Cyclin D1 binds to and activates cyclin-dependent kinases (CDK4). This complex phosphorylates RB and dissociates it from transcription factor (mainly E2F). Activated E2F mediates expression of several genes required for cell cycle transition from G1 to S phase.

- Hedefe yönelik tedavi SCC'de yeni bir tedavi modelidir
- Faz çalışmaları devam eden bir çok ajan vardır
- Cetuximab bu alanda en çok kabul edilen ajandır

Update of cetuximab for non-melanoma skin cancer.

[Wollina U.](#)

⊕ Author information

Abstract

INTRODUCTION: Non-melanoma skin cancer (NMSC) has become the most common malignancy in humans. Targeted therapies are recent developments for these tumors. Monoclonal antibody cetuximab has proven its efficacy and has improved tolerability compared to classical chemotherapy protocols, and this prompted us to analyze new data on the use of cetuximab in cutaneous NMSC.

Cetuximab

- Küratif tedavide tek başına veya radyoterapi ile kombine kullanıldığında
- Palyatif tedavide radyoterapi ile kombine kullanıldığında



Surveyi artırmakta

Hedefe yönelik tedavi ajanları

Anti-EGFR monoklonal antikorları

- Cetuximab
- Zalutumumab
- Panitumumab
- Nimotuzumab (h-R3mAb)
- ABT-806
- EGFR antisense

Diğer hedefe yönelik ajanlar

- Foretinib (c-met inhibitörü)
- Figitumumab, cixutumumab (Anti IGF-1R)
- Bevacizumab (Anti VEGF)

EGFR tyrosine kinase inhibitörleri (TKI)

- Erlotinib
- Gefitinib (ZD1839)

Multipl HER receptör blokerleri

- Lapatinib
- Afatinib
- Dacomitinib

VEGF kinase inhibitörleri ve multi-kinase inhibitörleri

mAbs veya mAbs mikstürünü hedefleyen ajanlar

- MEHD7945A
- Catumaxomab
- Ertumaxomab
- Sym004

Hedefe yönelik tedavi ajanlarının etki yolları

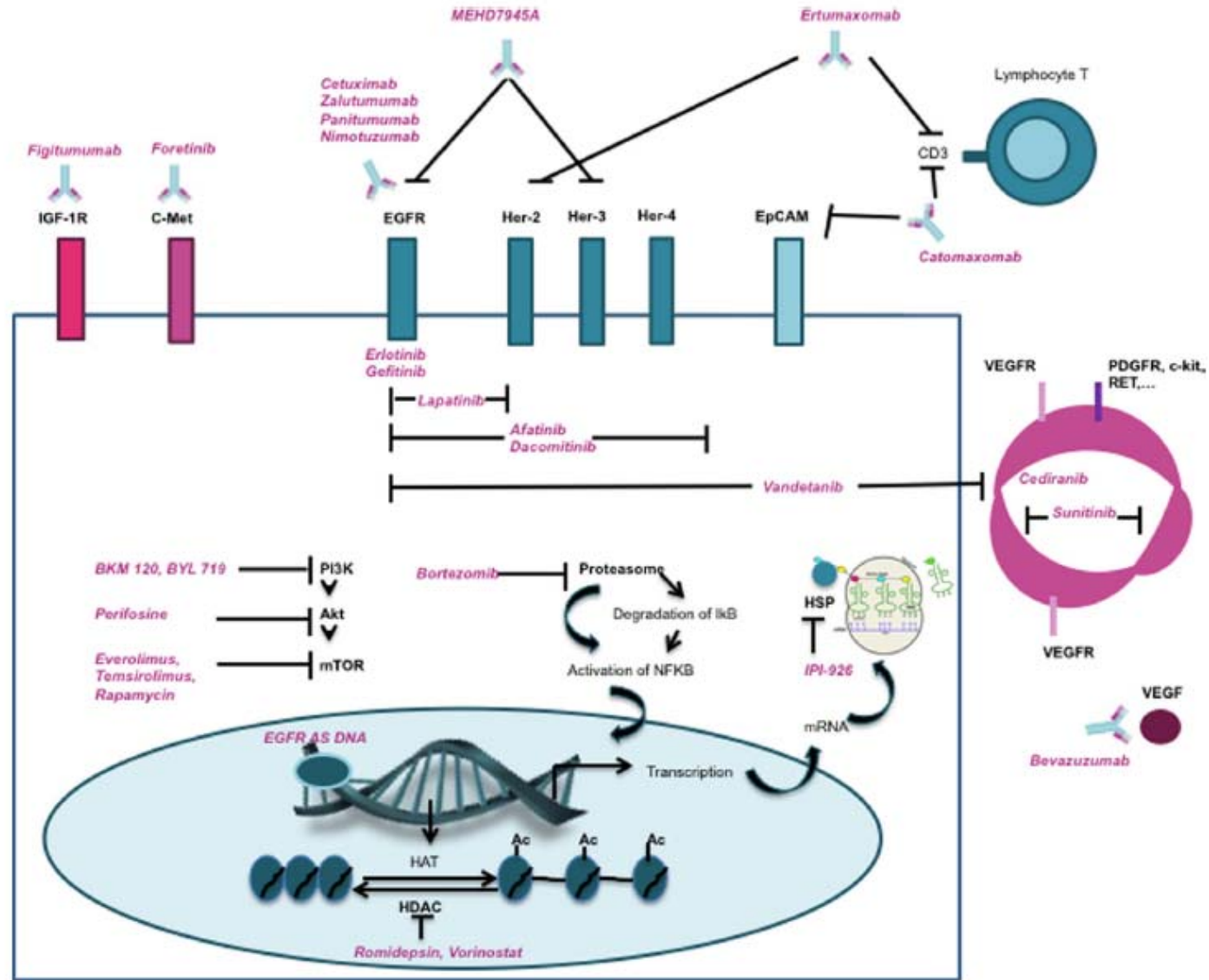


Fig. 1. Targeted agents in SCCHN.

SCC'de anti kanser ilaçların tedavi etkinliklerini artırmak amacıyla son yıllarda bir çok invivo ve invitro çalışma yapılmakta

A number of important studies recently been reported on head and neck cancer.

Study/agent	Mechanism/description	Results	Reference
Targeting STAT3	STAT3 decoy-mediated inhibition	Overcoming resistance to cetuximab, reduced cell viability	[41]
OSI-027/ASP4876	Inhibition of mTORC1/mTORC2	Enhanced sensitivity to EGFR inhibitors (cetuximab, erlotinib)	[6]
IKK α and β	Activation of NF- κ B/REL family transcription factors + activation of EGFR-AP1 pathway	Survival and migration of head and neck cancer cells	[30]
Chemotherapy (with cisplatin) + erlotinib	Clinical trial, study number: NCT00304278	Improved survival	[37]
miR145	Targeting SOX9 and ADAM17 axis + inhibition of IL-6 and sIL-6R	Inhibition of tumor-initiating cells + inhibition of IL-6-mediated paracrine effects	[56]
microRNA-29s	Inhibition laminin-integrin signaling	Inhibition of cell migration and invasion	[17]
Emodin	Inhibition of the beta-catenin and Akt pathways	Suppression of TWIST1-induced epithelial-mesenchymal transitions	[50]
miR-134	Targeting WWOX gene	Oncogenicity and metastasis	[25]
Atorvastatin	Inhibition of RhoC activity by preventing its geranylgeranylation	Reduced metastasis	[14]
let-7i	Repression of bone morphogenetic protein 4 (BMP4)	Decreased mesenchymal migration of cancer cells	[54]
siRNA	Inhibition of Lyn kinase (a member of Src family)	Decreased cell migration/invasion of EGFRvIII-expressing HNSCC	[52]
Docetaxel with or without gefitinib	Phase III trial in recurrent or metastatic HNC	Addition of gefitinib to docetaxel does not improve outcomes	[2]
Hydroxyurea (HU) + valproic acid (VPA)	Increasing the expression of BIM + decreasing EGFR expression and surface localization	Proliferation inhibition + BIM-dependent apoptosis	[46]
Acquired resistance to cetuximab	Overexpression of the K-Ras, H-Ras and N-Ras, amphiregulin and TGF α	Improved radiation efficiency in cetuximab-resistant cells by targeting Ras and PI3K activity	[40]
Resistance to radiation	Activation of PI3K/Akt pathway		

Notes: BIM, BCL-2 interacting mediator of cell death; HNC, head and neck cancer; IKK, inhibitor- κ B kinase; IKK-NF- κ B, inhibitor- κ B kinase-nuclear factor- κ B; SOX-9, a transcription factor; TWIST1, twist-related protein 1; WWOX, WW domain-containing oxidoreductase.

- Bu ilaçlarla ilgili en önemli problem kanser hücrelerinin bu ilaçlara karşı geliştirdiği direnç
- İleri çalışmalarda bu dirençlerin gösterilmesi ve buna yönelik stratejiler tedavi başarısını artıracaktır
- SCC'de antikanser ilaçların tedavi etkinliğini artırmak amacıyla birçok değerli deneysel bilgi elde edilmiş
- Bu bilgilerin hasta üzerindeki etkinliğini göstermek için çok sayıda klinik çalışmaya ihtiyaç var

TEŐEKKÜRLER

