Carcinogênese, Biologia dos Tumores e Marcadores Tumorais em Cirurgia de Cabeça e Pescoço

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Introdução

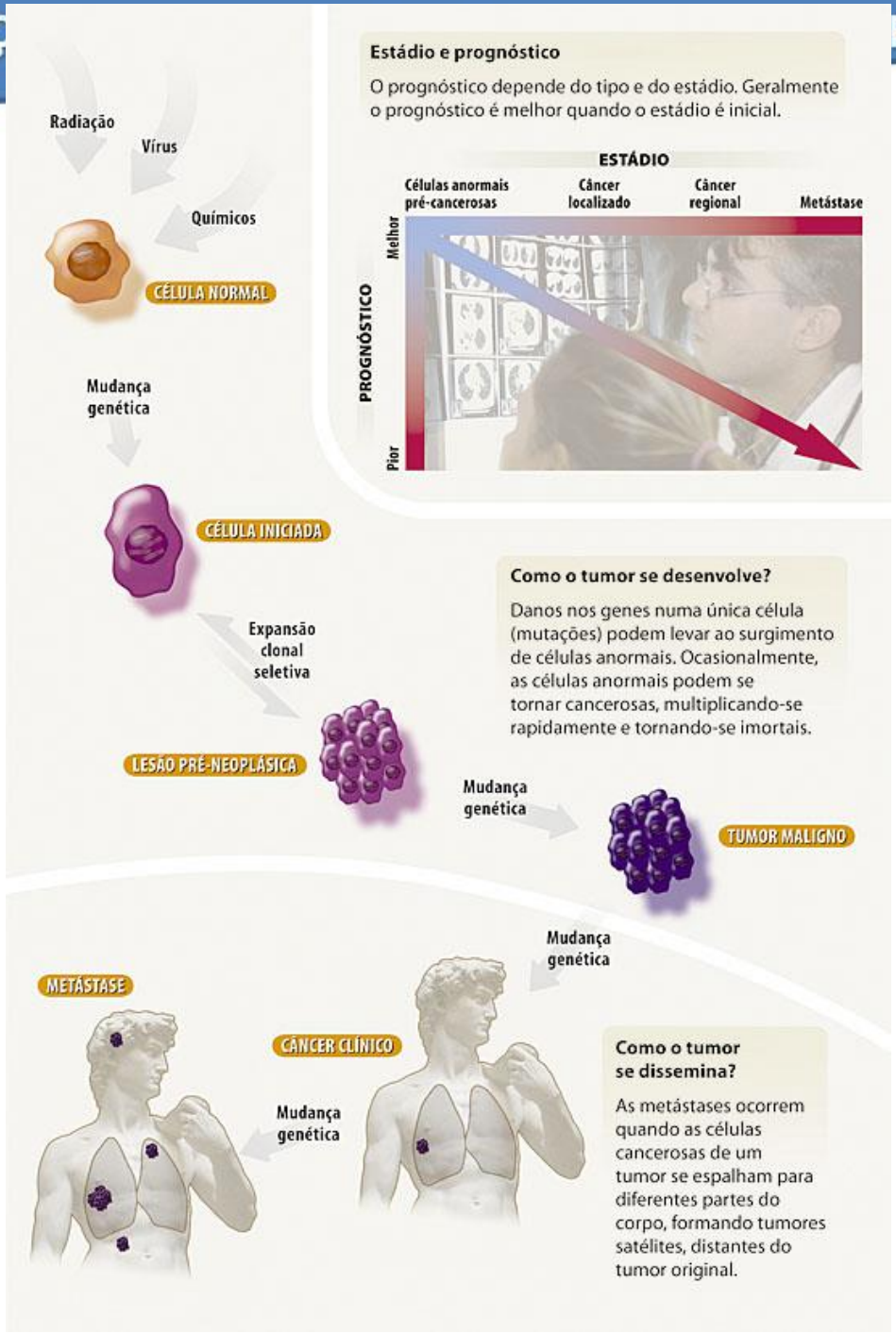
- CEC CP – Quinto câncer do mundo
- Fatores Carcinogênicos
  - Álcool, tabaco, HPV
- Síndromes Hereditárias
  - Anemia de Fanconi, Sd. de Li Fraumeni, Sd. de Bloom, Xeroderma Pigmentoso
- Suscetibilidade Genética
- Progressão por estágios patológicos

Carcinogênese

- Mutações acumuladas
- Crescimento clonal
- Protooncogenes
- Genes supressores

Carcinogênese

- Deleções mais comuns – 9p21, 3p, 17p21, 13q14, 4q, 6p, 7, 8, 14q e 19q
- 9p21 70%
- 3p 60%
- 17p 50% - correlação com p53


Radiação
Vírus
Químicos
CÉLULA NORMAL
Mudança genética
CÉLULA INICIADA
Expansão clonal seletiva
LESÃO PRÉ-NEOPLÁSICA
Mudança genética
TUMOR MALIGNO
Mudança genética
METÁSTASE
CÂNCER CLÍNICO
Mudança genética
Estádio e prognóstico
O prognóstico depende do tipo e do estádio. Geralmente o prognóstico é melhor quando o estádio é inicial.
ESTÁDIO
Células anormais pré-cancerosas
Câncer localizado
Câncer regional
Metástase
PROGNÓSTICO
Melhor
Pior
Como o tumor se desenvolve?
Danos nos genes numa única célula (mutações) podem levar ao surgimento de células anormais. Ocasionalmente, as células anormais podem se tornar cancerosas, multiplicando-se rapidamente e tornando-se imortais.
Como o tumor se dissemina?
As metástases ocorrem quando as células cancerosas de um tumor se espalham para diferentes partes do corpo, formando tumores satélites, distantes do tumor original.

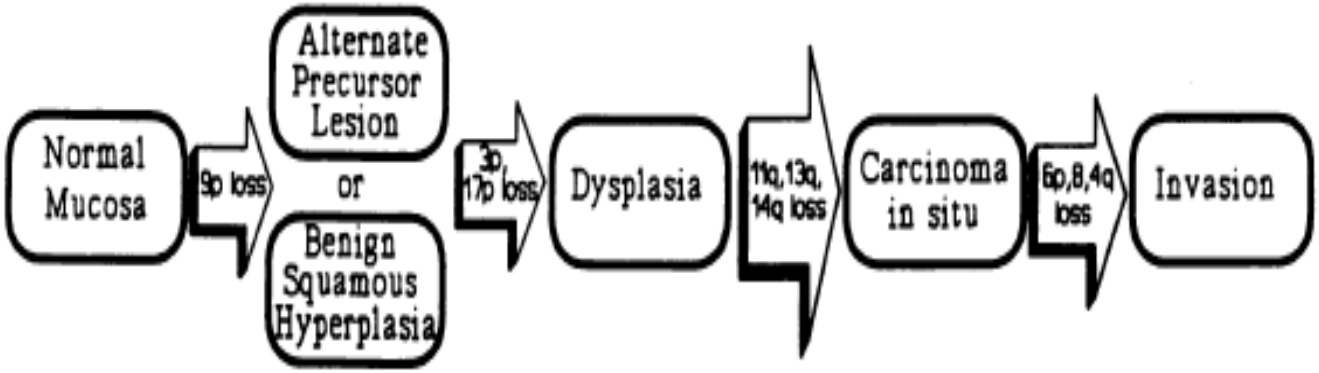


Fig. 3. Genetic progression of HNSCC. Genetic changes associated with the histopathological progression of HNSCC based on loss of chromosomal material (allelic loss). Genetic alterations have been placed prior to the lesion where the frequency of the particular event plateaus. It is the accumulation and not necessarily the order of genetic events that determines progression. A small fraction of benign squamous hyperplastic lesions contain 9p21 or 3p21 loss, suggesting that an unidentified precursor lesion (or cells) may also give rise to dysplasia. Candidate tumor suppressor genes include *p16* (9p21), *p53* (17p), and *retinoblastoma* (13q), and a candidate proto-oncogene includes *cyclin* D_1 (11q13).

Marcadores Tumorais

- Fatores de Crescimento Epitelial (EGFR, Her-2/neu, c-erbB3 e c-erbB4) – pior prognóstico, quimiorresistentes
- Ciclina D1 – progressão fase G1 – pior prognóstico, 30-50% CEC laringe
- Ki67 – indicador proliferação celular – maior TNM, metástases cervicais

Marcadores Tumorais

- Bcl-2 – antiapoptótica *
- Fas/FasL – mediadores apoptose *
- p27 – supressor tumoral – baixos níveis = pior prognóstico
- p53 – modulador resposta celular – freqüente alteração

Marcadores Tumorais

- VEGF – Neovascularização
  - A – angiogênese e permeabilidade vascular
  - B – funções pouco conhecidas
  - C e D – angiogênese e linfagiogênese
- Moléculas de adesão intercelulares – E-caderinas – presença de metástases
- Moléculas de adesão célula-substrato
  - Integrinas – expressão aberrante – invasão e meta
  - CD 44 – progressão para metástase

Marcadores Tumorais

- Enzimas proteolíticas – metaloproteínas
- Supressores de metástases – nm23 – associado a menor taxa de metástases

Aplicação Clínica

- 50% contêm gene HPV – menor mutação p53
- VEP – carcinoma nasofaríngeo
- Vacinas
- Estadiamento Molecular
- Diagnóstico e acompanhamento

Cancer Letters

journal homepage: www.elsevier.com/locate/canlet

The anti-EGFR antibody cetuximab sensitizes human head and neck squamous cell carcinoma cells to radiation in part through inhibiting radiation-induced upregulation of HIF-1α

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A B S T R A C T

In this study, we investigated the mechanisms underlying cetuximab-mediated radiosensitization of HNSCC. Irradiation of HNSCC cells upregulated hypoxia-inducible factor-1 alpha (HIF-1α) via a mechanism involving *de novo* synthesis of HIF-1α protein. Radiation-induced upregulation of HIF-1α was completely abolished by concurrent treatment of HNSCC cells with cetuximab. Experimental elevation of constitutively expressed HIF-1α abolished cetuximab-mediated radiosensitization in HNSCC cells, whereas downregulation of HIF-1α by siRNA or a small molecule inhibitor enhanced responses of cetuximab-resistant HNSCC cells to cetuximab plus radiation. Our data suggest that cetuximab sensitizes cancer cells to ionizing radiation in part through inhibition of radiation-induced upregulation of HIF-1α.

Acta Oto-laryngologica

Potential prognostic and therapeutic role for angiogenesis markers in laryngeal carcinoma

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Abstract

Angiogenesis is a hallmark of cancer, fundamental to its growth. The 'angiogenic switch' occurs when pro-angiogenic factors are not balanced by anti-angiogenic factors. A correlation between angiogenic properties and oncological prognosis (for laryngeal squamous cell carcinoma (LSCC) too) was first hypothesized in the 1990s. An exhaustive literature review was performed to investigate available data on angiogenesis markers and their biological role and therapeutic potential in LSCC. The prognostic significance of microvascular density in LSCC was investigated with endothelial targets, e.g. CD105, CD34, and CD31. Epidermal growth factor receptor (EGFR), vascular endothelial growth factor (VEGF), VEGF receptor 2, angiogenin, hypoxia-inducible factor 1, and other biological markers were also studied. Only anti-EGFR therapy has been approved by the USFood and Drug Administration (FDA) for head and neck carcinoma in recent years, while several agents interfering with VEGF and its receptors are being studied. Experimental findings indicate that anti-CD105 monoclonal antibodies efficiently inhibit tumor angiogenesis. There are two main ways to approach the vascular profile of solid malignancies: by inhibiting new vessel formation (anti-angiogenic therapy) or selectively damaging neoplastic vessels (vascular targeting therapy). In advanced LSCC, both these strategies seem promising and warrant further preclinical and clinical investigation.


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