

肺がんおよび悪性胸膜中皮腫の分子機構

肺がんの治療は医師人生 40 年の間で劇的な進化をみた。1979 年大学卒業時、抗癌剤は毒薬に近かった。益と不利益のバランスという考え方はこの当時はなかった。肺がん化学療法の主役である白金製剤シスプラチンは 1983 年に日本で承認されている。シスプラチン単独治療の限界は知られており、1990 年以降に承認された第三世代の抗がん薬の何を加えるのかが一時議論されていた。

2002 年 7 月、EGFR-TKI ゲフィチニブ（イレッサ®）が薬事承認を受けた。この当時は遺伝子変異、ドライバー遺伝子という考え方はなかった。EGFR 遺伝子変異は肺がんのドライバー遺伝子と同定され、それに対する分子標的治療薬として EGFR-TKI ゲフィチニブの有効性が証明された。同時に、有害事象としての薬剤性肺障害である肺線維症の発症が日本を揺るがす問題となった。肺がんドライバー遺伝子の同定が進み、次々と分子標的治療薬の開発が進んで 2020 年の時点に至っている。

がん細胞の免疫機構の異常（非自己と認識しない免疫機構）を制御する、がん免疫治療（免疫チェックポイント阻害薬）ニボルマブ（オプジーボ®）が 2014 年に薬事承認を受けた。テールブラトールというがん患者さんの長期生存が得られる可能性が示唆されている。2018 年ノーベル医学生理学賞を本庶佑 京都大学特別教授が受賞した。

肺がん (COPD) 検診
千葉大学病院呼吸器内科・興 浩一郎

肺癌は慢性閉塞性肺疾患・間質性肺炎などの呼吸器疾患が存在していると、高率に発症します。

千葉大学医学部附属病院呼吸器内科では千葉市の肺がん (COPD)・結核検診に対する精密検査を行っています。

受診後の流れ
精密検査で大学を受診
→ 胸部CTで精査
→ 気管支鏡・CTガイド下肺生検で診断
→ 治療方針の決定

喫煙者では肺がんの発症率が高くなります。呼吸機能検査で息をはく力が低下している慢性閉塞性肺疾患の方では、そうでない方と比べると、肺がんの発生率が5倍くらい高くなります。そのような方では、胸部CTによる精密検査を施行して、胸部X線写真だけでは見つけられない肺がんの早期発見に努力しています。

Respirology
Official Journal of the Asia Pacific Society of Respiratory

地域基盤型の肺がんスクリーニングにおける COPD の発見

ORIGINAL ARTICLE

Detection of chronic obstructive pulmonary disease in community-based annual lung cancer screening: Chiba Chronic Obstructive Pulmonary Disease Lung Cancer Screening Study Group

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Respirology 2014;19:98

呼吸器内科では、呼吸器外科・千葉県との協力の下、全国の自治体で初めて肺がん (COPD) 検診を導入した。肺がんの基礎疾患として COPD を発見して、その経過観察中に早期肺がんを発見して外科手術に持っていくという試みである。地域基盤型の肺がんスクリーニングにおける COPD 発見の可能性を検討した。60 歳以上の喫煙歴・呼吸器症状があった住民の約 30% は COPD の診断であった。COPD と診断された住民の半数は中等症・重症 COPD であったが、医療機関で診断・加療されている COPD 患者さんは極めて少数であった (Respirology 2014;19:98-104)。

アスベストの健康被害の一つである悪性胸膜中皮腫は数十年後に発現する。千葉県がんセンターの田川雅敏が主導で、世界で初めて「NK4 遺伝子発現ベクターを用いた悪性中皮腫の臨床研究」を施行した。NK4 は正常な細胞を傷つけず、がん細胞の増殖を抑制して栄養供給血管を断つという効果が期待された。呼吸器内科のがん免疫研究のかなりの部分は田川雅敏の指導によるものである。下記の【分子機構】業績に挙げるように、多田裕司が千葉県がんセンターの田川雅敏博士の指導を受けた時点から開始している。

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2016~17 千葉大学病院 TOPICS

世界初 NK4遺伝子でがん細胞を抑える TOPICS



世界初 NK4遺伝子でがん細胞を抑える!

千葉大学病院では世界で初めて「NK4遺伝子発現ベクターを用いた悪性中皮腫の臨床研究」を開始しました。NK4は正常な細胞を傷つけず、がん細胞の増殖を抑制する血管新生を誘導するという働きが期待されています。癌発生を抑制し、安全な遺伝子治療のベクターを、癌細胞に対してがん細胞に感染させると、中で合成されるNK4タンパク質ががん細胞の機能を低下させます。



「NK4遺伝子を用いてがん細胞の増殖を抑制!」
NK4遺伝子を用いてがん細胞の増殖を抑制! NK4遺伝子を用いてがん細胞の増殖を抑制! NK4遺伝子を用いてがん細胞の増殖を抑制!



左：千葉大学病院臨床研究 柳川博樹、研究員 藤原 多志朗



iMig 2016
Towards Personalized Care

悪性胸膜中皮腫臨床試験

1. NK4遺伝子発現型アデノウイルスベクターによる臨床研究
→ 全症例終了。御協力ありがとうございました。

2. ソレドロン酸の胸腔内投与の安全性確認第I相臨床試験
→ 引き続き症例募集中
切除不能悪性胸膜中皮腫症例



Molecular-Targeted Therapy For Malignant Mesothelioma

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