
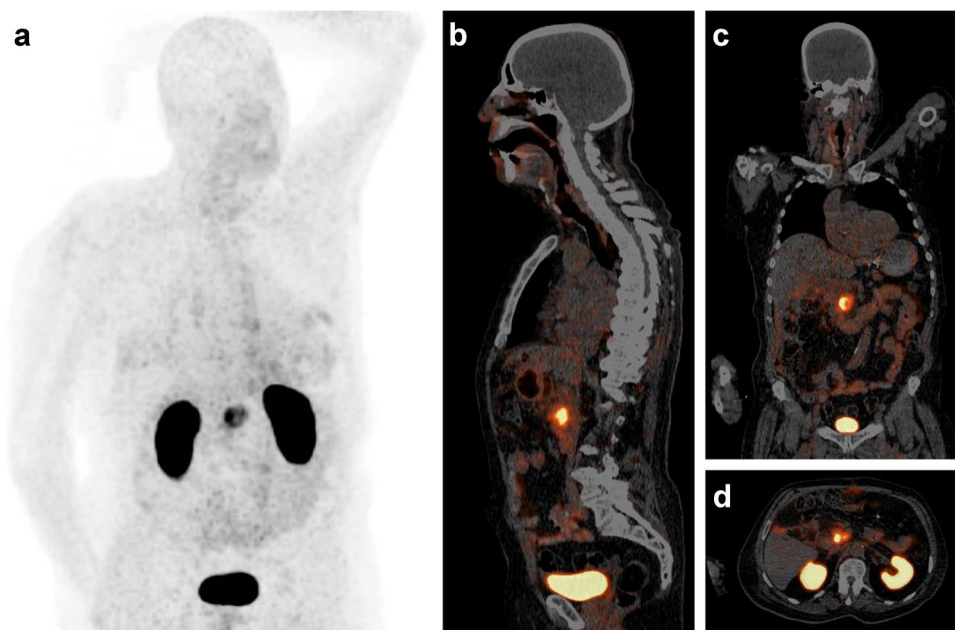




## PET/CT imaging of pancreatic carcinoma targeting the “cancer integrin” $\alpha\beta6$

Neil Gerard Quigley<sup>1</sup> · Norbert Czech<sup>2</sup> · Wolfgang Sendt<sup>3</sup> · Johannes Notni<sup>1,4</sup> 

Received: 2 April 2021 / Accepted: 31 May 2021 / Published online: 9 June 2021  
© The Author(s) 2021



$\alpha\beta6$ -Integrin is exclusively expressed by epithelial cells and plays an important role for invasion and metastasis of carcinomas. We found a high expression of  $\beta6$  on tumor cells

This article is part of the Topical Collection on Image of the month.

✉ Johannes Notni  
johannes.notni@uk-essen.de

- <sup>1</sup> Institute of Pathology, Technische Universität München, Trogerstr, 18, 81675 München, Germany
- <sup>2</sup> Center of Nuclear Medicine and PET/CT Bremen, Schwachhauser Heerstraße 54, 28209 Bremen, Germany
- <sup>3</sup> Clinic of Surgery, Hospital St. Joseph-Stift, Schwachhauser Heerstraße 54, 28209 Bremen, Germany
- <sup>4</sup> Experimental Radiopharmacy, Clinic for Nuclear Medicine, University Hospital Essen, Hufelandstr. 55, 45147 Essen, Germany

in 88% of nearly 400 specimens of pancreatic ductal adenocarcinoma (PDAC) primaries and in virtually all metastases [1]. We earlier reported a series of  $^{68}\text{Ga}$ - and  $^{177}\text{Lu}$ -labeled  $\alpha\beta6$ -integrin-specific cyclic nonapeptides, but found that despite some showed a good tumor-to-background contrast in rodent models, tumor accumulation was ultimately too low for a successful clinical transfer [2]. We hypothesized that trimerization might result in elevated target-specific uptake and prolonged retention and thus elaborated a trimerized  $\alpha\beta6$ -specific  $^{68}\text{Ga}$ -peptide named  $^{68}\text{Ga}$ -Trivehexin.

The image shows a  $^{68}\text{Ga}$ -Trivehexin PET/CT of a male patient (82 y, 89 kg) with a histologically confirmed PDAC in the pancreatic head (87 MBq, 70 min p.i., acquisition time 25 min, 0.7 mm/s, 3 min/bed position; anterior MIP (a) scaled to SUV 12; PET in slices (b–d) to SUV 10). Apart from the PDAC lesion ( $\text{SUV}_{\text{max}} = 13.1$ ), prominent signals are observed only in kidneys and urinary bladder due to renal

excretion. No relevant uptake is seen in lungs, stomach, liver, and intestines. In light of a limited value of [ $^{18}\text{F}$ ]FGD-PET for early detection of PDAC [3], we anticipate that  $^{68}\text{Ga}$ -Trivehexin will have a clinical value in this setting, besides the potential applications for fibrosis and other carcinomas (head-and-neck squamous cell, lung adenocarcinoma, colon, cervical, mammary) which have been addressed previously by  $\alpha\text{v}\beta\text{6}$ -integrin targeted PET-radiopharmaceuticals [4–6].

**Author contributions** Conceived and designed the experiment: NGQ, NC, WS, JN. Performed the experiments: NC, WS. Analyzed the data: NGQ, JN. Wrote the original manuscript: JN. All authors approved the final version of the manuscript.

**Funding** Open Access funding enabled and organized by Projekt DEAL. This work was funded by the Deutsche Forschungsgemeinschaft (SFB 824, project A10).

**Data availability** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval** Not applicable.

**Consent to participate** The authors affirm that the patient provided written informed consent prior to the investigation.

**Consent for publication** The authors affirm that the patient provided written informed consent for publication of the images.

**Competing interests** N.G.Q. and J.N. are co-inventors of patents related to  $^{68}\text{Ga}$ -Trivehexin. J.N. is shareholder of TRIMT GmbH (Radeberg, Germany), which is active in the field of radiopharmaceutical development.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

## References

1. Steiger K, Schlitter AM, Weichert W, Esposito I, Wester HJ, Notni J. Perspective of  $\alpha\text{v}\beta\text{6}$ -Integrin Imaging for Clinical Management of Pancreatic Carcinoma and Its Precursor Lesions. *Mol Imaging*. 2017;16:1536012117709384.
2. Färber SF, Wurzer A, Reichart F, Beck R, Kessler H, Wester HJ, et al. Therapeutic radiopharmaceuticals targeting integrin  $\alpha\text{v}\beta\text{6}$ . *ACS Omega*. 2018;3:2428–36.
3. Strobel O, Büchler MW. Pancreatic cancer: FDG-PET is not useful in early pancreatic cancer diagnosis. *Nat Rev Gastroenterol Hepatol*. 2013;4:203–5.
4. Roesch S, Lindner T, Sauter M, Loktev A, Flechsig P, Müller M, et al. Comparison of the RGD motif-containing  $\alpha\text{v}\beta\text{6}$  integrin-binding peptides SFLAP3 and SFITGv6 for diagnostic application in HNSCC. *J Nucl Med*. 2018;59:1679–85.
5. Hausner SH, Bold RJ, Cheuy LY, Chew HK, Daly ME, Davis RA, et al. Preclinical development and first-in-human imaging of the integrin  $\alpha\text{v}\beta\text{6}$  with [ $^{18}\text{F}$ ] $\alpha\text{v}\beta\text{6}$ -binding peptide in metastatic carcinoma. *Clin Cancer Res*. 2019;25:1206–15.
6. Kimura RH, Wang L, Shen B, Huo L, Tummers W, Filipp FV, et al. Evaluation of integrin  $\alpha\text{v}\beta\text{6}$  cystine knot PET tracers to detect cancer and idiopathic pulmonary fibrosis. *Nat Commun*. 2019;10:4673.

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.