The cellular and molecular interaction between tumor cells and platelets - role in diagnosis and tumor metastasis.

Published: 05-09-2018
Last updated: 11-04-2024

1. To investigate tumor-interaction properties and tumor-education of platelets from patients with GI cancers. 2. To expand our knowledge of phosphatase expressions pattern in GI cancers

Ethical review	Approved WMO
Status	Pending
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational invasive

Summary

ID

NL-OMON45896

Source
ToetsingOnline

Brief title
The role of platelets in gastrointestinal cancer.

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
cancer of the intestinal tract, gastrointestinal tumors

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: cancer, phosphatases, platelets, tumor-education

Outcome measures

Primary outcome

1. Tumor education of platelets from patients with GI cancers compared to healthy controls (mRNA profiles, activation status)

2. LMWPTP and PTP1B expressions pattern in oesophageal and gastric cancers and their precursor lesions compared to healthy tissue.

Secondary outcome

1. Aggregation and thrombus formation of platelets from GI patients in response to tumor cells in vitro will be compared between GI cancer patients and healthy controls

2. Expression of activation markers on platelets from patients with GI cancer and healthy controls in vitro induced by tumor cells with and without LMWPTP/PTP1B expression (knock down cell lines).

3. Investigation of the molecular pathways activated in tumor cells by activation with platelets from GI cancer patients vs healthy controls, including shedding of NKG2D ligands.

Study description

Background summary

Early identification of carcinogenesis and prevention of metastasis are two important clinical challenges for gastrointestinal tumors. The role of blood platelets in these processes is gaining interest. It has been shown that platelet activation state and platelet mRNA profiles in breast cancer patients

are significantly altred as compared to healthy controls, and studies are ongoing to investigate whether such tumor-education of platelets may be used for early identification of patients with breast cancer. In addition to tumor cell modulation of platelets, it has also been suggested that platelets can modulate tumor cells. Coating of tumor cells with platelets facilitates their migration, allows their escape from immunosurveillence by NK cells, amongst others by inducing shedding of NKG2D ligands from tumor cells. We have previously shown that several phosphatases (e.g. LMWPTP, PTP1B) are overexpressed in colorectal, prostate and haematological malignancies and confer cancer hallmarks. We have shown that LMPWTP decreases survival and promotes metastasis, and demonstrated in vitro that overexpression of this phosphatase affects tumor cell migration. Our preliminary data further suggest that platelets show increased interaction with tumor cells which express high levels of LMWPTP or PTP1B, indicating an advantage for cells expressing these phosphatases to metastasize. We have additionally shown that LMPWTP in platelets is upregulated in response to agonists in healthy controls, and thus may contribute to their reactivity and tumor education. To what extent phosphatases plays a role in the tumor education of platelets (TEP), and whether platelets from patients with gastrointestinal cancers show altered tumor-activating properties, is as yet unknown.

Study objective

1. To investigate tumor-interaction properties and tumor-education of platelets from patients with GI cancers.
2. To expand our knowledge of phosphatase expressions pattern in GI cancers

Study design

1. Molecular and cellular analysis of platelet activation behaviour in relation to LMWPTP and PTP1B expression will be studied by investigating platelet activation markers, tumor education and LMWPTP/PTP1B expression. Patients with esophageal, gastric, and colorectal cancer will be compared with eachother and healthy controls. Furthermore we will in vitro incubate platelets from patients with GI cancer and controls with tumor cell lines expressing high and low levels of LMWPTP/PTP1B and assess platelet aggregation patterns as well as molecular changes in both platelets and tumor cells.
2. FFPE sections of oesophageal and gastric cancer tissue as well as normal squamous esopgeal tissue and gastric tissue will be stained for LMWPTP and PTP1B expression. These tumors show high metastatic potential, and are therefore expected to carry high levels of these phosphatases, as was previously demonstrated for colorectal cancer.

Study burden and risks

Participants will be asked to donate blood (3 tubes) during routine clinical

visits. The burden and risk of this study is therefore negligible. FFPE sections will be identified from the PALGA database, and no new biopsies are required for this study. The study is expected to yield insight into tumor metastasis biology, thrombosis risk and may provide support for diagnostic cancer hallmarks in the form of tumor-educated platelets, which may help predict patients at risk for metastasis in the future. Metastasis of disease is particularly common in GI cancer, and is the major cause of death. Prevention of metastasis is expected to contribute to improved patient survival.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015CE
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015CE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Confirmed gastrointestinal tumor: esophageal, stomach or colorectal cancer.

Treatment naive.

Exclusion criteria

Not able to give informed consent.
Treatment with anticoagulants.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2018
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO

Date:	05-09-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL66029.078.18