SCHEMA DI CONVENZIONE per la realizzazione del Work Package 7 "Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests" – Programma di rete NET-2016-02363853 "Performance evalutation and value assessment for cardiovascular and oncological care path in a regional network context: challenges and opportunities" finanziato nell'ambito del Bando Ricerca Sanitaria Finalizzata 2016 del Ministero della Salute.

Premesso che

gli articoli 12 e 12 bis del D.Lgs. 502/1992, come modificato dal D.Lgs.n. 229/1999, stabiliscono che una quota del Fondo Sanitario Nazionale sia destinata al finanziamento di attività di ricerca sanitaria al fine di rispondere al fabbisogno conoscitivo e operativo del Servizio Sanitario Nazionale e disciplinano lo svolgimento delle relative attività individuando i soggetti Destinatari Istituzionali (D.I.) che possono concorrere alla realizzazione dei progetti di ricerca, quali le Regioni;

in data 20.06.2016 il Ministero della salute ha pubblicato il "Bando Ricerca Finalizzata 2016" articolato in due principali aree di ricerca, change-promoting e theory-enhancing, ed in cinque categorie di progetti, tra cui i Programmi di Rete (NET);

il sopracitato Bando prevede che i Programmi di Rete siano articolati in non meno di tre e non più di otto Work Package ed abbiano lo scopo di creare gruppi di ricerca e innovazione per lo sviluppo di studi altamente innovativi e caratterizzati dall'elevato impatto sul SSN, finalizzati a soddisfare le esigenze di programmazione regionale e di sviluppo dei servizi per il miglioramento dell'assistenza e delle cure offerte; il Bando prevede, altresì, che i Programmi di Rete siano finanziati dal Ministero della Salute e dalle Regioni che hanno a tal fine stipulato specifico Accordo di Collaborazione;

le Regioni Lombardia, Liguria, Toscana, Umbria e Veneto finanziano la tematica di Programma di Rete n. 3 "Strumenti standardizzati per la validazione delle performance delle aziende sanitarie, la valutazione di efficienza ed efficacia dei percorsi di cura erogati e la strutturazione di percorsi di audit clinico per il miglioramento della qualità delle cure incluse le emergenze cardio e cerebrovascolari" come da Accordo di collaborazione di cui alla DGR n. 858 del 7.06.2016;

a seguito dell'approvazione della graduatoria dei Programmi di Rete presentati, sulla base delle determinazioni assunte dal Comitato Tecnico Sanitario, il Ministero della Salute, con nota prot. n. 839 del 8.2.2018, ha comunicato ai Destinatari Istituzionali Regioni Lombardia (Regione Capofila), Liguria, Toscana, Umbria e Veneto che, nell'ambito della tematica n. 3 sopracitata, è risultato collocato nell'area di finanziamento il Programma di Rete NET-2016-02363853 "Performance evalutation and value assessment for cardiovascular and oncological care path in a regional network context: challenges and opportunities";

il predetto Programma è articolato nei seguenti otto Work Package (WP):

- WP 1: "Dynamic feedback auditing methods to support quality improvement of healthcare organizations" – Grande Ospedale Metropolitano Niguarda (Ente SSN capofila) Principal Investigator del WP1 e Coordinatore del Programma Prof. Salvatore Siena;
- WP 2: "Assessing care paths, effectivenss and cost-effectiveness from real world data" – Università degli Studi di Milano Bicocca – Principal Investigator Prof. Giovanni Corrao;
- WP 3: "Appraisal and remodelling of acute coronary syndrome and heart failure models of care: towards a patient-centered approach" – Fondazione Toscana Gabriele Monasterio – Principal InvestigatorProf. Michele Emdin;
- WP 4: "Patient value assessment and multi-dimensional performance evaluation of integrated care paths: breast and cardiovascular care" – Scuola Superiore di Studi Universitari e di Perfezionamento Sant'Anna – Principal Investigator Prof. Vincenzo Lionetti;

- WP 5: "Improving healthcare quality through performance indicators of cardiovascular diseases" – Azienda Ospedaliera di Perugia Santa Maria della Misericordia –Principal Investigator Dott. Giuseppe Ambrosio;
- WP 6: "Monitoring recommendations on innovative oncology drugs: development, adherence, clinical outcomes and pharmacoeconomical impact" – IRCCS Istituto Oncologico Veneto – Principal Investigator Prof. Pierfranco Conte;
- WP 7: "Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests" – Università degli Studi di Padova – Dipartimento di Medicina – DIMED – Principal Investigator Prof. Massimo Rugge;
- WP 8: "Outcome measures, process measures and clinical audits for monitoring clinical performance and quality of care in cancer networks: the case of cancer survival" – IRCCS AOU San Martino-IST – Principal Investigator Dott. Paolo Bruzzi;

il finanziamento assegnato, come da Programma approvato, è il seguente:

- Ministero della Salute: complessivi Euro 2.851.700,00 ai WP 1, 3, 5, 6 e 8 afferenti al Servizio Sanitario Nazionale;
- Regione Lombardia: Euro 600.000,00 al WP 2;
- Regione Toscana: Euro 150.000,00 al WP3; Euro 448.897,00 al WP 4;
- Regione Umbria: Euro 600.000,00 al WP 5;
- Regione Veneto: Euro 595.499,00 al WP 7;
- Regione Liguria: Euro 600.000,00 al WP 8;

la soprarichiamata nota del Ministero prescrive, ai fini della stipula della convenzione attuativo dell'intero Programma di Rete, la sottoscrizione e l'invio al Ministero della Salute di copia della convenzione attuativa tra ciascuna Regione finanziatrice e l'Ente nel cui ambito sono svolte le attività di ricerca del WP di competenza della Regione stessa;

a tal fine si rende necessario stipulare una Convenzione tra la Regione del Veneto e l'Università degli Studi di Padova – Dipartimento di Medicina – DIMED – sottoscritta anche per presa visione dal Principal Investigator – per regolare i reciproci rapporti inerenti il finanziamento regionale del WP 7: "Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests" secondo lo schema approvato con la DGR n.…… del ……..;

Tutto ciò premesso e ritenuto parte integrante e sostanziale del presente atto, tra

REGIONE DEL VENETO

rappresentata da ……, nato/a a …..… il … e domiciliato/a per la carica in Venezia, Dorsoduro 3901, che interviene al presente atto non per sé, ma in nome e per conto della Giunta regionale del Veneto, con sede in Venezia, Dorsoduro 3901, codice fiscale n. 80007580279, nella sua qualità di ……..…, a ciò autorizzato dalla DGR n. ….....del ……;

e

UNIVERSITA' DEGLI STUDI DI PADOVA
DIPARTIMENTO DI MEDICINA – DIMED

rappresentata da …….. nato/a a ……..…il ……., che interviene al presente atto non per sé, ma in nome e per conto dell'Università di Padova – Dipartimento di Medicina – DIMED, con sede in ……..., codice fiscale n ……..… nella sua qualità di ……..,

si conviene e si stipula quanto segue.

ART. 1

1. La presente convenzione regola i reciproci rapporti inerenti il finanziamento regionale tra la Regione del Veneto e l'Università degli Studi di Padova – Dipartimento di Medicina – DIMED, presso cui si svolgeranno le attività di ricerca relative al WP 7 "Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests" del Programma di Rete NET-2016-02363853 con Principal Investigator il Prof. Massimo Rugge.

2. Il Principal Investigator svolgerà presso l'Università degli Studi di Padova – Dipartimento di Medicina – DIMED – come da Piano Esecutivo approvato dal Ministero della Salute e di cui all'Allegato A parte integrante della presente convenzione, coordinandosi con i Principal Investigator degli altri WP del Programma e in ottemperanza a quanto previsto dal Bando Ricerca Finalizzata 2016.

3. Le eventuali proposte di variazione finanziaria relative al finanziamento, comprovanti che le modifiche sono richieste per assicurare il raggiungimento degli obiettivi e indispensabili per la realizzazione della ricerca, dovranno essere sottoposte dall'Università degli Studi di Padova – Dipartimento di Medicina – DIMED alla Regione del Veneto entro 120 giorni la scadenza originaria o prorogata del Programma di Rete e avranno effetto solo dopo l'approvazione da parte della Regione del Veneto.

ART. 2

1. La ricerca ha la durata di 3 anni a decorrere dalla data di inizio dell'attività che verrà individuata secondo le modalità stabilite dalla convenzione attuativa dell'intero Programma che verrà stipulata tra il Ministero della Salute, la Regione Lombardia (Regione capofila), il Grande Ospedale Metropolitano Niguarda (Ente del Servizio Sanitario Nazionale capofila) e, per presa visione, il Prof. Salvatore Siena, Coordinatore del Programma.

2. Le attività del WP 7 sono finanziate dalla Regione del Veneto per un importo massimo di Euro 595.499,00 (fuori del campo di applicazione IVA) come da scheda finanziaria di cui al Piano esecutivo del WP allegato (Allegato 1).

3. L'Università degli Studi di Padova – Dipartimento di Medicina – DIMED si impegna a consentire al Principal Investigator di svolgere le attività di ricerca previste per l'intero periodo di attuazione del Programma, assicurando il necessario supporto tecnico, logistico, amministrativo e contabile.

ART. 3

1. Il finanziamento regionale sarà corrisposto, per il tramite di Azienda Zero ai sensi dell'articolo 2., comma 1, lettera b, della L.R. 19/2016, all'Università degli Studi di Padova – Dipartimento di Medicina – DIMED – con le seguenti modalità:

a) la prima rata, pari al cinquanta per cento (50%) del finanziamento, a seguito dell'avvio delle attività di ricerca;
b) la seconda rata, pari al trenta per cento (30%), in considerazione degli esiti della valutazione della relazione scientifica intermedia e del rendiconto delle spese sostenute con il finanziamento regionale;
c) il saldo, massimo venti per cento (20%), in considerazione degli esiti della valutazione della relazione scientifica finale e del rendiconto delle spese sostenute con il finanziamento regionale.

ART. 4

1. Entro il termine di trenta (30) giorni dalla scadenza del diciottesimo (18°) mese di attività, per

l'erogazione della seconda rata, l'Università degli Studi di Padova – Dipartimento di Medicina - DIMED deve trasmettere alla Regione la relazione scientifica intermedia sullo stato di attuazione della ricerca e il rendiconto delle spese sostenute con il finanziamento regionale.

2. Entro il termine di trenta (30) giorni dalla data di scadenza della ricerca, naturale o prorogata, l'Università degli Studi di Padova – Dipartimento di Medicina – DIMED - deve trasmettere alla Regione del Veneto la relazione scientifica conclusiva che deve dimostrare la coerenza dell'attività complessivamente svolta, gli obiettivi raggiunti e i documenti prodotti e il rendiconto delle spese sostenute con il finanziamento regionale.

3. La documentazione amministrativo - contabile deve essere resa disponibile per ogni ulteriore attività di controllo e deve essere conservata agli atti dell'Università degli Studi di Padova – Dipartimento di Medicina - DIMED.

ART. 5

1. I diritti di proprietà intellettuale inerenti i risultati dell'attività di ricerca sono regolamentati dalla normativa vigente in materia e dagli accordi e dalle convenzioni stipulati per la realizzazione del Programma di Rete.

2. Qualsiasi documento o prodotto, ivi comprese le pubblicazioni scientifiche, inerenti al Programma deve contenere l'indicazione che gli stessi sono stati ottenuti con il finanziamento della Regione del Veneto.

3. Il Ministero della Salute e la Regione finanziatrice potranno dare direttamente diffusione, anche attraverso il proprio sito web, dei risultati della ricerca sia in forma completa che sintetica e delle pubblicazioni scientifiche prodotte. A tal proposito, ciascuna delle parti firmatarie conviene che l'obbligo di riservatezza nel trattamento dei risultati acquisiti nell'ambito della ricerca è fondamentale nell'espletamento dell'attività relativa all'utilizzo ed allo sfruttamento degli stessi, ivi compreso l'eventuale deposito di titoli di proprietà intellettuale ad essi correlati.

ART. 6

1. In caso di mancata o irregolare attuazione da parte del Principal Investigator o dell'Università degli Studi di Padova – Dipartimento di Medicina – DIMED, di quanto previsto dalla presente convenzione e dal piano esecutivo del WP (Allegato 1) la Regione attiva le procedure per la sospensione del finanziamento e, previa verifica delle cause che hanno determinato la mancata o irregolare realizzazione delle attività, il recupero delle somme già erogate.

ART. 7

1. La presente convenzione ha decorrenza dalla data di apposizione dell'ultima firma e durata sino alla conclusione, naturale o prorogata, della ricerca.

2. Le Parti si impegnano all'osservanza, per quanto di rispettiva competenza, delle disposizioni inerenti la tracciabilità dei flussi finanziari contenute nell'art. 3 della Legge 13 agosto 2010 n. 136, e successive modifiche e integrazioni, e delle disposizioni sul Codice Unico di Progetto di cui alla Legge 16 gennaio 2003, n. 3.

3. La Convenzione sarà oggetto di registrazione solo in caso d'uso con spese a carico del richiedente secondo le disposizioni fiscali vigenti in materia.

4. Per qualunque controversia in merito all'esecuzione della presente Convenzione, qualora non sia possibile esperire accordo extragiudiziale, il foro competente sarà quello di Venezia.

5. Sono a carico dell'Università degli Studi di Padova – Dipartimento di Medicina - DIMED tutte le spese, imposte e tasse inerenti e conseguenti alla stipula della presente Convenzione.

La presente convenzione è sottoscritta con firma digitale, ai sensi dell'articolo 24 del decreto legislativo 7 marzo 2005, n. 82, con firma elettronica avanzata, ai sensi dell'articolo 1, comma 1, lettera q-bis), del decreto legislativo 7 marzo 2005, n. 82, ovvero con altra firma elettronica qualificata.

Venezia, lì (data della sottoscrizione come quella dell'ultima firma digitale apposta).

PER LA REGIONE DEL VENETO

PER L'UNIVERSITA' DEGLI STUDI DI PADOVA
DIPARTIMENTO DI MEDICINA - DIMED

Per presa visione
Il Principal Investigator
Prof.

Allegato 1 alla Convenzione

Piano esecutivo del WP 7 - NET-2016-02363853-7

Titolo: “Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests”.

(testo estratto dal Programma di Rete NET-2016-02363853 dal titolo “Performance evalutation and value assessment for cardiovascular and oncological care path in a regional network context: challenges and opportunities” approvato dal Ministero della Salute).

Ministero della Salute Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti BANDO 2016 PROGETTO COMPLETO		**Project Title:** Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests	
Project Code:	NET-2016-02363853-7	**Principal Investigator:**	RUGGE Massimo
Research Type:	c) Change-promoting: valutare i fattori professionali, organizzativi e di sistema che condizionano efficacia ed efficienza dei servizi sanitari e/o l'impatto sulla qualità di innovazioni cliniche, organizzative, gestionali e di finanziamento; Sviluppo...	**Applicant Institution:**	Veneto

Project Type: WP PROJECT - 7

Project Classification IRG: Healthcare Delivery and Methodologies

Project Classification SS: Health Services Organization and Delivery - HSOD

Project Keyword 1: Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoeconomics.

Project Keyword 2:

Project Keyword 3:

Project Request: **Animals:** ☐ **Humans:** ☐ **Clinical trial:** ☐

The object/s of this application is/are under patent copyright Y/N: ☐

Investigators, Institution and Role in the Project

	Co-PI	Key Personnel	Institution/Org./Pos.	Role in the project	Birth Date
1	X	Fassan Matteo	AOU Padova, UOC Anatomia Patologica	CoPI	28/08/1980
2		Marco Pizzi	Dipartimento di Medicina (DIMED) Università degli Studi di Padova	Expert Research Collaborator	26/08/1985
3		Pennelli Gianmaria	Dipartimento di Medicina (DIMED) Università degli Studi di Padova	Expert Research Collaborator	16/08/1972

Overall Summary

The future of precision medicine is in targeting the cancer genetic paths with medications, immuno-therapies, DNA sequencing. Cancer profiling (histology, immunohistochemistry, genetics) is essential for both correct management of therapeutic protocols, and decisions about cost-effective oncological therapies. In such a landscape, the spectrum of the diagnostic procedures have a strategic impact. In several Italian Regions, as well as in the Veneto, multidisciplinary experts groups have put forward consensus protocols for clinically dealing with the diagnostic/therapeutic procedures of the most incident cancer histotypes (Diagnostic-Therapeutic Paths [DTPs]). The DTPs also list a number of ¿patho-biological indicators (Path-KI) of the diagnostic performance (i.e. gross reporting, histology, immunohistochemistry [IHC], molecular profiling). WP7 aims to monitor the consistency between the diagnostic DTP-recommendations and their implementation in the oncology real-world practice.

Background / State of Art

For personalized anticancer therapies, the precision medicine requires both solid histology phenotyping and consistent molecular profiling. Moreover, companion diagnostics are prerequisites for a cost-effective use of targeted drugs. As a consequence, precision diagnostics (from histology to molecular profiling) currently play a key role in precision medicine. As in other Italian Regions, also the Veneto oncology network (Regional Oncology Networks [RONs]) has recently established a number of DTPs, specifically detailing the diagnostic/therapeutic procedures to be applied for most incident cancers (1,2). The DTPs primarily aim to: i) standardize the diagnostic/therapeutic procedures; ii) personalize the patients¿ management according with the available scientific evidence; iii) efficiently allocate resources.

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Project Type: WP PROJECT - 7

All DTPs include well-defined patho-biological indicators of the diagnostic performances, including gross reporting, histology phenotyping, immunohistochemistry, and molecular profiling. However, no information is available on: i) the inter-regional consistency of the DTPs documents (diagnostic approach, therapeutic choices); ii) how and if the DTPs' recommendations are currently applied at each local/regional level, iii) the efficacy of the patho-biological indicators in monitoring the diagnostic workflow.

Hyphotesis and Specific AIMS

Hyphotesis and Significance:

Different Italian Health Care Regional Systems (HCRSs) have established multi-task oncology networks (RONs) for the cancers¿ clinical management. The RONs¿ experts have put forward a number of Diagnostic-Therapeutic Paths (DTPs) detailing the diagnostic/therapeutic procedures for most incident neoplasia.

No information is available on the impact of DTPs in the oncology diagnostic practice. Systematically testing how the DTPs are applied in real-world oncology may result in: i) DTPs clinical validation; ii) monitoring the diagnostic performances; iii) identification of points of fragility/strength, as assessable by the available Path-KIs; iv) validation of the chosen Path-KIs; v) assessment of how, a DPT-based clinical management may improve the efficiency of HCRSs.

Preliminary Data:

The Padua University has a solid experience on the patho-biological cancer profiling. This background guarantees: i) multidisciplinary teams of oncologists; ii) cooperative efforts with Regional Institutions (WP6); iii) significant interaction with the Veneto Cancer Registry (the PI of WP7 is the Scientific Director of the registry).

The Veneto-RON has issued several DTPs for most incident cancers (breast, colorectal, gastro-esophageal), which include specific patho-biological key-indicators (Path-KI) of the cancer assessment.

Examples of Path-KI in colorectal cancer (3): i) histology assessment of the pT1 cancers; ii) number of dissected nodes (12) from surgical specimens; iii) nodal metastatic/non-metastatic ratio; iv) histology assessment of the MSI-status; v) prevalence of RAS mutated tumors in M1 cancers.

Examples of Path-KI in breast cancer (4): i) time elapsed from the biopsy sampling to the histology reporting; ii) IHC profiling (as included in the histology report: ER, PR, Ki67, HER2); iii) FISH-procedures; iv) consistency of the sentinel lymph node procedure.

Examples of Path-KI in gastroesophageal cancer (5): i) number of biopsy samples for HER2-status assessment; ii) structure of histology report; iii) gross cancer assessment on resected specimens; iv) histology assessment of the efficacy of neoadjuvant therapies; v) FISH-procedures; vi) the nodal metastatic/non-metastatic ratio.

Specific Aim 1:

This stepwise research project includes: i) preliminary testing the the DTPs inter-regional consistency; ii) assessment of the performance of the diagnostic procedures by systematically measuring indicators of the diagnostic Path-KI; iii) corrective interventions addressing the patho-biological cancer profiling (more efficient diagnostic tests, new diagnostic Path-KIs, educational interventions promoting inter-institut

Aim 1: To assess the inter-Regional consistency of the oncology-DTPs for breast, gastric, and colorectal cancer.

Specific Aim 2:

Aim 2: To explore the coherence between the 3 diagnostic paths, as established by the DTPs, and the real world practice, with elective focus on the inter-institutional consistency in the phenotypic/molecular cancer profiling.

Ministero della Salute Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti BANDO 2016 PROGETTO COMPLETO		Project Title: Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests	
Project Code:	NET-2016-02363853-7	**Principal Investigator:**	RUGGE Massimo
Research Type:	c) Change-promoting: valutare i fattori professionali, organizzativi e di sistema che condizionano efficacia ed efficienza dei servizi sanitari e/o l'impatto sulla qualità di innovazioni cliniche, organizzative, gestionali e di finanziamento; Sviluppo...	**Applicant Institution:**	Veneto

Project Type: WP PROJECT - 7

Specific Aim 3:

Aim 3: To make uniform the diagnostic procedures among the different Oncology institutions, by promoting both corrective interventions and educational policies.

Experimental Design Aim 1:

To assess the inter-Regional consistency of the oncology-DTPs for breast, gastric, and colorectal cancer.
The inter-regional consistency of the DTPs contents, however, has never been tested yet. Aimed to assess the clinical coherence of the different regional-DTPs, the addressed DPTs will be systematically compared. This comparison (essential for any further more detailed research) will address the major steps of the diagnostic patho-biological procedures.
Diagnostic Path-KIs will include: i) pre-surgical histology/cytology reporting; ii) post-surgical profiling (gross, histology); iii) post-surgical IHC profiling; iv) molecular post-surgical profiling.

Experimental Design Aim 2:

To explore the coherence between the 3 diagnostic paths, as established by the DTPs, and the real world practice, with elective focus on the inter-institutional consistency in the phenotypic/molecular cancer profiling.
Based on multicenter cohorts of cancer patients (as obtained by Cancer Registries of the involved WPs), the following issues will be addressed: a) quantification of the consistency between the ideal diagnostic workflow (as established by the DTPs) and the real world diagnostic oncology practice; b) inter-institutional consistency in the cancer pathobiology assessment (histology, molecular profiling in both biopsy and/or surgical specimens, timing of the molecular profiling).
- The inter-institutional consistency of the pathology assessment will be tested by addressing the pathology reports as issued by different institutions. Different cancer types (breast, colorectal, gastric) will be considered to investigate the coherence of the pathology reporting (as issued at different Institutions) with the DTPs-guidelines.
- The molecular profiling will be specifically addressed. In randomly selected case, both the IHC (predictive biomarkers) and the molecular profile will be retested to validate the original results. The status of predictive biomarkers (IHC) will be tested on automated stainers (Leica Biosystems, Ventana, Dako); the molecular testing will be performed on both traditional Sanger sequencing/Sequenom MassArray technology and Ion Ampliseq next generation sequencing technology.

Experimental Design Aim 3:

D.3.3. Aim 3: ¿To amalgamate the diagnostic procedures among the different Oncology institutions, by promoting both corrective interventions and educational policies.
The clinical impact of any inconsistency in the cancer assessment will be addressed. The analysis will focus on the impact of the diagnostic phase on the timing/efficiency of the therapies (by appropriate Path-KIs, the cancer patients treated according to the DTPs will be compared with those managed outside the DTPs).
Based on the obtained results (Aims 1-2), corrective interventions will be proposed to optimize the histology/molecular diagnostic procedures: i) critical reappraisal of the diagnostic indicators; ii) introduction of alternative diagnostic Path-KIs; iii) testing novel predictive biomarkers (IHC/ISH) and/or novel cancer-specific multigene hotspots next generation sequencing panels.
To increase the level of intra- inter-Regional consistency in the procedures of cancer assessment, educational interventions will promote the inter-regional networking aimed to apply similar diagnostic procedures.

Picture to support preliminary data:

Preliminary data.pdf

Ministero della Salute Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti BANDO 2016 PROGETTO COMPLETO		Project Title: Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests	
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Project Type: WP PROJECT - 7

Metodologies and statistical analyses:

Clinical information, Patho-biology cancer assessment:

All studies involving human material/data will be submitted for approval to the Ethics Committee. Gross pathology reports and the original specimens will be jointly reassessed by two pathologists. A representative sample (at least 500 cases per tumor type) will be considered, allowing consistent calculations on 6-8 variables to be included in multivariate models (also in dealing with low-prevalent variables).

IHC/ISH will be performed on automated stainers (Leica Biosystems, Ventana, Dako). Sanger sequencing will be performed for selected exons of several genes with prognostic/ predictive clinical relevance on ABI Prism 3500 Genetic Analyzer. Hotspot multigene sequencing will be performed by using the Sequenom MassArray platform and Diatech diagnostic kits. Multiplex PCR amplification and Deep sequencing will be performed on Ion AmpliSeqTM technology on an Ion ProtonTM (Life Technologies).

Epidemiological cancer data (incidence, prevalence, demographics) will be obtained by the interaction with Cancer Registries (the WP7- PI is the current scientific Director of the Veneto Cancer Registry).

Statistics:

For each diagnostic Path-KI, the following items will be established: a) unequivocal definition, as prerequisite of consistent measurements; b) data necessary to its computation and data-sources; c) mathematical formula for calculations; d) reference values.

The study population will include adults with breast, colorectal, and gastric cancers as assessed during the study period. Incident cases will be identified by using both hospitalization and pathology databases. Residence will be defined by record linkage with the regional database. The different Path-KIs (see above) will be calculated on the basis of the data collected from the different data-sources. The reliability of the results obtained of those indicators achieved only from routine administrative datasets (hospitalization and outpatient databases) will be assessed by comparing them with a reference-standard represented by a sample of cases whose clinical documentation will be directly accessed.

Each of the considered Path-KIs will be calculated at: a) each single Diagnostic Unit (also distinguished according to the patients¿ volume); b) Hub and Spoke Health care Institutions (as defined by the RON); c) calendar period.

All the assessments will cover not less than 24 months.

Appropriate statistics will be applied to test differences among the variables. Funnel plots will be used to describe the performance at each diagnostic Unit level, and intra- inter-regional variability as a function of the volume of managed patients.

Within the same and among different Regions, the study will also explore (multivariate models) the association between any increased risk of failure in complying with DTP-guidelines, and variables: a) patient-related (age, gender, etc.), b) operator-related (patients volume during the observation period); c) Unit-related (Different HCRSs; Hub versus Spoke hospitals, etc).

Expected outcomes:

Aim 1: To assess the inter-Regional consistency of the oncology-DTPs for breast, gastric, and colorectal cancer. To systematically explore both the inter-regional consistency of the DTPs and their clinical implementation will result into more defined information on the state-of-art on the cancer patients¿ care (essential prerequisite for resources allocation).

Aim 2: To explore the coherence between the 3 diagnostic paths, as established by the DTPs, and the real world practice, with elective focus on the inter-institutional consistency in the phenotypic/molecular cancer profiling. By acquiring information on the points of weakness/strengths of the oncology diagnostic workflow, the project will result in efficiently harmonizing the diagnostic with the therapeutic steps.

Aim 3: To amalgamate the diagnostic procedures among the different Oncology institutions, by promoting both corrective

Ministero della Salute Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti BANDO 2016 PROGETTO COMPLETO		Project Title: Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests	
Project Code:	NET-2016-02363853-7	**Principal Investigator:**	RUGGE Massimo
Research Type:	c) Change-promoting: valutare i fattori professionali, organizzativi e di sistema che condizionano efficacia ed efficienza dei servizi sanitari e/o l'impatto sulla qualità di innovazioni cliniche, organizzative, gestionali e di finanziamento; Sviluppo...	**Applicant Institution:**	Veneto

Project Type: WP PROJECT - 7

interventions and educational policies. By endorsing the (intra- inter-regional) consistency of the diagnostic procedures, the project is expected to promote the efficiency/efficacy of the DTPs-performances.

Risk analysis, possible problems and solutions:
A pilot-survey on diagnostic Path-KIs will be performed on the data achievable from the involved Regional Cancer Registries. The significant bias resulting form missing data will be overcome by auditing the involved Pathology Units at each regional institution. Referenced personnel will manage the collection of missing data.
The cancers molecular profiling is expected as major point of inconsistency. Molecular tests are mostly based on paraffin-embedded tissue, potentially affecting DNA/RNA quality. Possible solutions:
- Fixation DNA-damage generating nicks/gaps, oxidizing bases blocking the 3 ends, and fragmenting/cross-linking DNA. Several methods have been proposed to overcome DNA degradation (uracil N-glycosylase-based kits). Before sequencing analysis we will test 3 of them on a series of ¿pilot¿ samples to be run on a custom panel using Sequenom MassArray technology.
- Because of it may not be possible to design an assay for Sequenom MassArray and Ion Ampliseq sequencing for every hotspot of interest, the multigene panels will be integrated by Sanger sequencing of the uncovered regions.
- To overcome tumor heterogeneity, the molecular profile will be assessed on the same tissue samples used for the original tests.

Significance and Innovation

Successful innovation in clinical Oncology is much more interactive, involving many institutions and processes. In the clinical oncology practice, the implementation of the Diagnostic Therapeutic Paths ([DTPs] as established in different Italian Regions) is currently restricted to a limited number of Health care Institutions. WP7 aims to monitor if and how the diagnostic procedures, as included in the DTPs, are applied at the ¿operative level (intra-regional and inter-regional variability). Specifically addressing the diagnostic phase of the neoplastic diseases, the project is basically aimed to increase the inter-institutional consistency of the cancer biological profiling (i.e. the networking as driver of the operative innovation). As adjunctive aim, the project will also explore the clinical implementation of novel, reproducible, companion diagnostic tests to identify patients who can benefit from targeted therapies.

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Project Type: WP PROJECT - 7

Description of the complementary and sinergy research team

Synergy within WP7:
The profile of the WP7-researchers is consistent with the expected complementary expertises: a) the PI is Director of Cancer Registry (source of epidemiology cancer data); b) Dr Fassan is expert in cancer patho-biology; c) Dr Pennelli is expert in cancer histology/IHC. The synergy among these competences will be harmonised with the technical, administrative, informatics competences as available at the research site.
WP7s synergy with other WPs (see D4):
- synergy with WP1: audit-methodology within regional clinical networks;
- synergy with WP2: protocols for collection/analysis of real-world data (platform generating real-world evidence);
- synergy with WP3: the method for testing the path performance in chronic heart failure (audits) will be also exploited for collecting/analyzing the Path-KIs of the diagnostic oncology procedures;
- synergy with WP6: bridging the diagnostic with the therapeutic path (impact of the diagnostic phase on the clinical outcome)

Training and tutorial activities

Training, tutorial and (more in general) educational activities are intended as structural parts of the project. To increase the level of the inter-institutional diagnostic biological consistency needs both consensus-documents and personal interactions. Both actions will be systematically taken consistently with the purpose of establishing diagnostic paths similar among all the involved intra- and inter-regional realities.

Bibliography

1. https://salute.regione.veneto.it/web/rov/gruppi-di-lavoro
2. https://salute.regione.veneto.it/web/rov/coordinamento-rete-oncologica-veneta
3. https://salute.regione.veneto.it/web/rov/colon
4. https://salute.regione.veneto.it/web/rov/mammella
5. https://salute.regione.veneto.it/web/rov/pdta-stomaco

Timeline / Deliverables / Payable Milestones

Timeline and Deliverables are attached in the GANTT EXCEL file

Milestones 18 month

Report on the state-of-art on the cancer patients¿ care (colon, breast, gastric cancers) systematically evaluating DTPs' intra- and inter-regional performance

Milestones 36 month

Report on the clinical impact of cancer diagnostic assessment within the network of the research project. Report on the corrective interventions. Coclusion of the educational activities

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Project Code:	NET-2016-02363853-7	**Principal Investigator:**	RUGGE Massimo
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Project Type: WP PROJECT - 7

Gantt chart

WP7 Timeline GANTT.xlsx

Equipment and resources available

The studies will be carried out at the Anatomic Pathology Department - Department of Medicine (DIMED) of the Padua University. The Anatomic Pathology Department of the Padova University is one of the largest in Europe, performing annually more than 58,000 histological diagnosis, 150 autopsy procedures, and 30,000 cytological tests. The Unit is fully equipped for: i) histological processing biological tissue samples; ii) IHC and in situ hybridization analyses; iii) morphometric analysis (Leica SCN400 [Leica Microsystems GmbH, Wetzlar, Germany] and Cyres system [Zeiss, Jena, Germany]); iv) genetic analysis and mutational screening (PCR, qRT-PCR, Sanger sequencing, Pyrosequencing and Sequenom sequencing) on FFPE tissue samples. Along with bench and office spaces, the Unit is provided with -20, and -80 freezer. The Anatomic Pathology Department of the Padua University supports with its clinical data the Cancer Registry of Veneto Region, covering a regional population of 3.500.000 inhabitants. The research group has full access to the epidemiological data collected by the Registry. The current Scientific Director of the Cancer Registry is the PI of this WP7.
All the involved researchers have full access to all the facilities.

Translational relevance and impact for the National Health System (SSN)

DTPs have been recently produced by different regional (multidisciplinary) oncology networks (RONs). This national network project will result into a fundamental detail on the state-of-art of the clinical oncology among the involved Regions. In particular, the National Health System will be provided by a basic information on "if and how" the oncology diagnostic procedures (as established by the DTPs) are applied at the ¿operative level¿ (intra-regional and inter-regional variability). This information will allow more informed strategy, more efficient allocation, and even alternative re-allotment of the available resources. As adjunctive benefit, the clinical implementation of novel, reproducible, companion diagnostic tests will result in a more consistent identification of those cancer patients who can benefit from targeted therapies, with significant curtail of the economic burden of National Health Service.

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Research Type: c) Change-promoting: valutare i fattori professionali, organizzativi e di sistema che condizionano efficacia ed efficienza dei servizi sanitari e/o l'impatto sulla qualità di innovazioni cliniche, organizzative, gestionali e di finanziamento; Sviluppo...	**Applicant Institution:** Veneto

Project Type: WP PROJECT - 7

PRINCIPAL INVESTIGATOR PROFILE

Name		
RUGGE Massimo	Institution	Veneto
	Department/Unit	DEPARTMENT OF MEDICINE UNIVERSITY OF PADOVA (DIMED)
	Position Title	FULL PROFESSOR OF PATHOLOGY

Education/Training - Institution and Location	Degree	Year(s)	Field of study
University of Edinburgh	Visiting Professor	0	Liver oncology
Catholic University of Leuven Belgium	Visiting Professor	0	Liver oncology
Padova University	Specialist in Oncology	2	Oncology
Genova University	Specialist in Pathology	3	Anatomic pathology
School of Medicine; Padova University	Medical Doctor	6	Medicine

Personal Statement

At the Padova University, he is full professor of Pathology and Dean of the University School of Diagnostic Sciences. He is currently adjunct professor of Medicine at the Baylor College of Medicine, USA. He has been recruited as WHO consultant. He is Director of the Veneto Cancer Registry and President of the Regional Bioethics Committee. His main scientific interest is neoplastic pathology. He authored more than 400 scientific articles. As PI of this WP, he will be involved in evaluation, monitoring, and critical reappraisal of the indicators of the diagnostic workflow in oncology patients.

Positions and Honors

Institution	Division / Research group	Location	Position	From year	To year
Baylor College of Medicine Houston- TX-USA	Department of Gastroenterology & Medicine	Baylor College of Medicine Houston- TX	Adjunct Professor of Medicine Department of Medicine	1998	2016
University of Padova	Department of Pathology	University of Padova	Full professor of Pathology; Chair of the Pathology department	2001	2016
University of Padova	Department of Pathology	University of Padova	Associate professor of Pathology	1985	2000

Grant, Awards and Honors

Official H index: 55.0

Source: Scopus **Scopus Author Id:** 7004614542

ORCID ID: 0000-0002-0679-0563 **RESEARCH ID:** K-7525-2016

Awards and Honors:

Italian Governor dell'American College of Gastroenterology (2003-2005)
Dean of the University School of ¿Sciences of Diagnostic Techniques¿ (2014-present).
President of the Italian College of Academic Pathologists (2015-present).

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Project Type: WP PROJECT - 7

Director of the Veneto Cancer Registry (2016-present).
President of the Regional Bioethics Committee (2016-present).

Other CV Informations:

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Ministero della Salute
Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti

BANDO 2016 PROGETTO COMPLETO

Project Title: Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests

Project Code: NET-2016-02363853-7

Principal Investigator: RUGGE Massimo

Research Type: c) Change-promoting: valutare i fattori professionali, organizzativi e di sistema che condizionano efficacia ed efficienza dei servizi sanitari e/o l'impatto sulla qualità di innovazioni cliniche, organizzative, gestionali e di finanziamento; Sviluppo...

Applicant Institution: Veneto

Project Type: WP PROJECT - 7

Selected peer-reviewed publications of the PI

Valid for PI minimum expertise level

Title	Publication / Journal	Pag	Vol	Year	DOI	PMID	IF	Cit.	P.*
Gastric epithelial dysplasia in the natural history of gastric cancer: a multicenter prospective follow-up study. Interdisciplinary Group on Gastric Epithelial Dysplasia	Gastroenterology	1288-96	107 (5)	1994	10.1016/0016-5085(94)90529-0	7926493	18.187	163	F
Gastric precancerous lesions: heading for an international consensus	Gut	15-18	45 (1)	1999	10.1136/gut.45.2008.i5	10457028	14.921	59	L
Microsatellite instability and/or loss of heterozygosity in young gastric cancer patients in Italy	Int J Cancer	59-62	82 (1)	1999	10.1002/(SICI)1097-0215(19990702)82:1<59::AID-IJC11>3.0.CO;2-2	10360821	5.531	18	L
Gastric dysplasia: the Padova international classification	Am J Surg Pathol	167-76	24(2)	2000	10.1097/00000478-200002000-00001	10680883	4.951	276	F
Review article: pre-neoplastic states of the gastric mucosa--a practical approach for the perplexed clinician	Aliment Pharmacol Ther.	43-50	15 suppl. 1	2001	10.1046/j1365-2036.2001.00110.x	11488661	6.32	25	L
The long term outcome of gastric non-invasive neoplasia	Gut	1111-6	52(8)	2003	10.1136/gut.52.8.1111	12865267	14.921	110	F
Gastritis staging in clinical practice: the OLGA staging system	Gut	631-6	56(5)	2006	10.1136/gut.2006.106666	17142647	14.921	149	F
Secondary prevention of gastric cancer	Gut	1646-7	56 (12)	2007	10.1136/gut.2007.133926	17998318	14.921	16	F
Oxidative DNA damage in gastric cancer: CagA status and OGG1 gene polymorphism.	Int J Cancer	51-5	123 (1)	2008	10.1002/ijc.23473	18366059	5.531	44	L
Bronchopulmonary carcinoid: phenotype and long-term outcome in a single-institution series of Italian patients	Clin Cancer Res	149-54	14 (1)	2008	10.1158/1078-0432.CCR-07-1631	18172265	8.738	41	F

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BANDO 2016 PROGETTO COMPLETO

Project Title:
Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests

Project Code: NET-2016-02363853-7

Principal Investigator: RUGGE Massimo

Research Type: c) Change-promoting: valutare i fattori professionali, organizzativi e di sistema che condizionano efficacia ed efficienza dei servizi sanitari e/o l'impatto sulla qualità di innovazioni cliniche, organizzative, gestionali e di finanziamento; Sviluppo...

Applicant Institution: Veneto

Project Type: WP PROJECT - 7

Title	Publication / Journal	Pag	Vol	Year	DOI	PMID	IF	Cit.	P.*
Inflammatory myofibroblastic tumor as adverse outcome of eosinophilic esophagitis	Endoscopy	E95-6	41 (Suppl. 2)	2009	10.1055/s-2008-1077646	19396747	5.634	1	L
Gastritis OLGA-staging and gastric cancer risk: A twelve-year clinico-pathological follow-up study	Aliment Pharmacol Ther.	1104-11	31(10)	2010	10.1111/j.1365-2036.2010.04277.x	20180784	6.32	96	F
MicroRNA expression profiling in human Barrett's carcinogenesis	Int J Cancer	1661-70	129(7)	2011	10.1002/ijc.25823	21128279	5.531	71	L
Isolated tumor cells in regional lymph nodes as relapse predictors in stage I and II colorectal cancer	J Clin Oncol.	965-71	30(9)	2012	10.1200/JCO.2011.35.9539	22355061	20.982	18	L
Clinical guidelines: Secondary prevention of gastric cancer	Nat Rev Gastroenterol Hepatol.	128-9	9(3)	2012	10.1038/nrgastro.2012.19	22330815	14.435	16	F
Barrett's esophagus and adenocarcinoma risk: the experience of the North-Eastern Italian Registry (EBRA)	Ann Surg.	788-95	256(5)	2012	10.1097/SLA.0b013e3182737a7e	23095623	8.569	22	F
Re: Risk of malignant progression in Barrett's esophagus patients: results from a large population based study	J Natl Cancer Inst.	1771-2	104 (22)	2012	10.1093/jnci/djs426	23042934	12.583	9	F
Transcribed ultraconserved noncoding RNAs (T-UCR) are involved in Barrett's esophagus carcinogenesis	Oncotarget	7162-71	5(16)	2014	10.18632/oncotarget.2249	25216530	5.008	4	L
Atrophic Gastritis in the Arctic	Clin Gastroenterol Hepatol	1601-3	13(9)	2015	10.1016/j.cgh.2015.05.016	25998786	7.68	2	L
Chronicles of a cancer foretold: 35 years of gastric cancer risk assessment	GUT	721-5	65(5)	2016	10.1136/gutjnl-2015-310846	26927528	14.921	0	F

* Position: F=First L=Last C=Corrispondent

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Ministero della Salute
Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti
BANDO 2016 PROGETTO COMPLETO

Project Title:
Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests

Project Code:	NET-2016-02363853-7	**Principal Investigator:**	RUGGE Massimo
Research Type:	c) Change-promoting: valutare i fattori professionali, organizzativi e di sistema che condizionano efficacia ed efficienza dei servizi sanitari e/o l'impatto sulla qualità di innovazioni cliniche, organizzative, gestionali e di finanziamento; Sviluppo...	**Applicant Institution:**	Veneto

Project Type: WP PROJECT - 7

For evaluation CV

Title	Publication / Journal	Pag	Vol	Year	DOI	PMID	IF	Cit.
p53 Alteration in gastric precancerous lesions	Am J Pathol	511-7	144 (3)	1994	--	8129036	4.206	189
Gastric epithelial dysplasia in the natural history of gastric cancer: a multicenter prospective follow-up study.	Gastroenterology	1288-96	107 (5)	1994	10.1016/0016-5085(94)90529-0	7926493	18.187	163
Oxidative DNA damage accumulation in gastric carcinogenesis	Gut	351-6	42 (3)	1998	10.1136/gut.42.3.351	9577340	14.921	189
Gastric dysplasia: the Padova international classification	Am J Surg Pathol	167-176	24 (2)	2000	10.1097/00000478-200002000-00001	10680883	4.951	276
Gastric mucosal atrophy: Interobserver consistency using new criteria for classification and grading	Aliment Pharmacol Ther.	1249-59	16 (7)	2002	10.1046/j.1365-2036.2002.01301.x	12144574	6.32	188
The long term outcome of gastric non-invasive neoplasia	Gut	1111-6	52(8)	2003	10.1136/gut.52.8.1111	12865267	14.921	110
Germ-layer specification and control of cell growth by ectodermin, a Smad4 ubiquitin ligase	Cell	87-99	121 (1)	2005	10.1016/j.cell.2005.01.033	15820681	28.71	188
Gastritis staging in clinical practice: the OLGA staging system	Gut	631-6	56(5)	2006	10.1136/gut.2006.106666	17142647	14.921	149
Gastritis OLGA-staging and gastric cancer risk: A twelve-year clinico-pathological follow-up study	Aliment Pharmacol Ther.	1104-11	31(10)	2010	10.1111/j.1365-2036.2010.04277.x	20180784	6.32	96
Management of Helicobacter pylori infection - The Maastricht IV/ Florence consensus report.	Gut	646-64	61 (5)	2012	10.1136/gutjnl-2012-302084	22491499	14.921	944

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Project Type: WP PROJECT - 7

Grant

Funded Institution / Country	Year	Title	Position in Projects	Fund (€)	Source / Funding Inst.	Att.*
University of Padua ¿ Padua, Italy	2014	Clinical utility of plasma-based miRNA signature classifiers in Barrett's carcinogenesis	Collaborator	41139	University of Padua ¿ Padua, Italy	No
University of Padova, Italy	2012	Tumor microenvironment and tumor spread in gastrointestinal cancers	Coordinator	750000	Renoval AIRC REGIONAL RESEARCH PROGRAM 2008 - AIRC (Italian Association for Cancer Research) & Fondazione Cassa di Risparmio Padova e Rovigo ¿ Padua, Italy	No

* Attached Certification Letter

Certification letter:

Ministero della Salute Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti BANDO 2016 PROGETTO COMPLETO	**Project Title:** Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests
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Project Type: WP PROJECT - 7

Biographical Sketch Contributors 1

Name:
Fassan Matteo

Institution	AOU Padova, UOC Anatomia Patologica
Department/Unit	Department of Medicine (DIMED) ¿ Surgical Pathology Unit
Position Title	CoPI

Education/Training - Institution and Location	Degree	Year(s)	Field of study
University of Padua, Padua - Italy	PhD in Oncology and Oncological Surgery	3	Medicine
University of Padua, Padua - Italy	Surgical Pathology Residency Program	5	Medicine
University of Padua, Padua - Italy	MD	6	Medicine

Personal Statement:

As cancer researcher with expertise in the molecular pathology and histopathology of the gastrointestinal and respiratory tracts, he will support the systematic collection of retrospective/prospective histopathology data and their interpretation. Moreover, his expertise and experience in molecular diagnostics will be essential for the planning of the molecular studies to be performed in the frame of the whole Network Project and the interpretation of the obtained results. Finally, he will assist in the exploitation and dissemination

Institution	Division / Research group	Location	Position	From year	To year
University of Padua	Prof Massimo Rugge	Padua (PD) - Italy	Assistant Professor of Pathology	2014	2016
Ohio State University	Prof. Carlo M. Croce	Columbus, OH - USA	Visiting Scholar	2013	2013
University of Verona	Prof. Aldo Scarpa	Verona (VR) ¿ Italy	Research Assistant	2012	2014
Thomas Jefferson University	Prof. Raffaele Baffa	Philadelphia, PA ¿ USA	Research Fellow	2006	2007

Awards and Honors

Official H index: 28.0

Source: Scopus **Scopus Author Id:** 20733941800

ORCID ID: 0000-0001-6515-5482 **RESEARCH ID:** F-5152-2012

Awards and Honors:

2012- Managing Editor, Frontiers in Bioscience
2013- Associate Editor, World Journal of Gastroenterology
2013- Associate Editor, World Journal of Respirology
2013 Board of Advisors, Hungarian Scientific Research Fund (OTKA)
2013 Selected abstract ¿ 10th International Gastric Cancer Congress

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Project Type: WP PROJECT - 7

2014 Associate Editor, BMC Gastroenterology
2014 Board of Advisors, Italian Society of Surgical Pathology ¿ GI pathology team
2015 Jeremy Jass Prize for Research Excellence in Pathology

Ministero della Salute Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti BANDO 2016 PROGETTO COMPLETO	**Project Title:** Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests
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Project Type: WP PROJECT - 7

Biographical Sketch Contributors 2

Name:		
Marco Pizzi	Institution	Dipartimento di Medicina (DIMED) Università degli Studi di Padova
	Department/Unit	: Department of Medicine-DIMED, Surgical Pathology & Cytopathology Unit
	Position Title	PhD Student

Education/Training - Institution and Location	Degree	Year(s)	Field of study
University of Padua, Padua-Italy	PhD Program in Biomedical Sciences	3	Tumor Metabolism and Mitochondrial Physiology
University of Padua, Padua-Italy	Residency Program in Surgical Pathology	5	Surgical Pathology& Cytopathology
University of Padua, Padua-Italy	Medical degree	6	Medicine

Personal Statement:

As surgical pathologist, he will be actively involved in the selection and evaluation of the main histopathological features for each case included within the project. Moreover, he will be involved in the evaluation of immunohistochemical and histochemical tests. Despite his young age, he has a well-documented experience in gastrointestinal pathology under the supervision of the PI (Prof. M. Rugge). At present, he is PhD student in Biomedical Sciences, and he is looking to transfer his clinical background into translational research

Institution	Division / Research group	Location	Position	From year	To year
Weill Cornell Medical College	Division of Hematopathology	New York (NY-USA)	Visiting Fellow	2014	2015
Sant¿Orsola-Maplighi Hospital	Hematopathology Unit	Bologna (BO-Italy)	Visiting Resident	2011	2015

Awards and Honors

Official H index: 15.0

Source: Scopus **Scopus Author Id:** 36021951700

ORCID ID: 0000-0003-4006-7317 **RESEARCH ID:** H-6273-2016

Awards and Honors:

Lundbeck s.p.a. Young Researcher Award for best graduation thesis in Medicine, June 2011 (Padova ¿Italy)

Ministero della Salute Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti BANDO 2016 PROGETTO COMPLETO	**Project Title:** Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests
Project Code: NET-2016-02363853-7	**Principal Investigator:** RUGGE Massimo
Research Type: c) Change-promoting: valutare i fattori professionali, organizzativi e di sistema che condizionano efficacia ed efficienza dei servizi sanitari e/o l'impatto sulla qualità di innovazioni cliniche, organizzative, gestionali e di finanziamento; Sviluppo...	**Applicant Institution:** Veneto

Project Type: WP PROJECT - 7

Biographical Sketch Contributors 3

Name:		
Pennelli Gianmaria	Institution	Dipartimento di Medicina (DIMED) Università degli Studi di Padova
	Department/Unit	Department of Medicine (DIMED) ¿ Surgical Pathology Unit
	Position Title	Assistant Professor of Pathology

Education/Training - Institution and Location	Degree	Year(s)	Field of study
University of Padua, Padua - Italy	Surgical Pathology Residency Program	5	Medicine
University of Padua, Padua - Italy	MD	9	Medicine

Personal Statement:

Expert surgical pathologist with elective experience in the histological and clinical characterization of the preneoplastic lesions of the gastrointestinal tract and of the thyroid gland. At present, he is Assistant Professor of Surgical Pathology at Padua University. He will support the systematic collection of retrospective/prospective histopathology data and their interpretation. Moreover, he will assist in the exploitation and dissemination

Institution	Division / Research group	Location	Position	From year	To year
University of Padua, Padua - Italy	Prof. Massimo Rugge	Padua, PD -Italy	Surgical Pathologist	2009	2016
Istituto Oncologico Veneto (IOV-IRCCS)	Prof. Massimo Rugge	Padua, PD -Italy	Surgical Pathologist	2006	2009

Awards and Honors

Official H index: 18.0

Source: Scopus **Scopus Author Id:** 6603933711

ORCID ID: 0000-0003-0210-165X **RESEARCH ID:** J-9937-2016

Awards and Honors:

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Expertise Research Collaborators

Selected peer-reviewed publications of the Research Group / Collaborators

Collaborator	Title	Publication / Journal	Pag	Vol	Year	DOI	PMID	IF	Cit.
Fassan Matteo	Effect of pathologic tumor response and nodal status on survival in the medical research council adjuvant gastric infusional chemotherapy trial	Journal of Clinical Oncology	Epub ahead of print	Epub ahead of print	2016	10.1200/JCO.2015.65.7692	27298411	20.982	0
Fassan Matteo	MicroRNA-135b promotes cancer progression by acting as a downstream effector of oncogenic pathways in colon cancer	Cancer Cell	469-483	25	2014	10.1016/j.ccr.2014.03.006	24735923	23.214	54
Fassan Matteo	Targeted next-generation sequencing of cancer genes dissects the molecular profiles of intraductal papillary neoplasms of the pancreas	Journal of Pathology	217-217	233	2014	10.1002/path4344	24604757	7.381	53
Fassan Matteo	Next-generation histopathologic diagnosis: a lesson from a hepatic carcinosarcoma	Journal of Clinical Oncology	e63-6	32	2014	10.1200/JCO.2012.47.5855	24493719	20.982	15
Fassan Matteo	Exome sequencing identifies frequent inactivating mutations in BAP1, ARID1A and PBRM1 in intrahepatic cholangiocarcinomas	Nature Genetics	1470-1473	45	2013	10.1038/ng.2813	24185509	31.616	111
Fassan Matteo	microRNA-145 in Barrett's oesophagus: regulating BMP4 signalling via GATA6	Gut	664-75	62	2013	10.1136/gutjnl-2011-301061	22504665	14.921	22
Fassan Matteo	Isolated tumor cells in regional lymph nodes as relapse predictors in stage I and II colorectal cancer	Journal of Clinical Oncology	965-971	30	2012	10.1200/JCO.2011.35.9539	22355061	20.982	18
Marco Pizzi	MicroRNA expression profiling in human Barrett's carcinogenesis	International Journal of Cancer	1661-1670	129	2011	10.1002/ijc.25823	21128279	5.531	71
Fassan Matteo	MicroRNA expression profiling of human metastatic cancers identifies cancer gene targets.	Journal of Pathology	214-21	219	2009	10.1002/path.2586	19593777	7.381	288
Pennelli Gianmaria	Galectin-3-expression analysis in the surgical selection of follicular thyroid nodules with indeterminate fine-needle aspiration cytology: a prospective multicentre study.	Lancet Oncology	543-9	9	2008	10.1016/S1470-2045(08)70132-3	18495537	24.725	153

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Project Type: WP PROJECT - 7

Grant

Funded Institution / Country	Year	Title	Position in Projects	Fund (€)	Collaborator	Source / Funding Inst.	Att.*
University of Padua ¿ Padua, Italy	2014-2016	Clinical utility of plasma-based miRNA signature classifiers in Barrett's carcinogenesis	Collaborator	41139	Marco Pizzi	University of Padua, http://www.unipd.it/ricerca/finanziamenti/finanziamenti-ateneo/progetti-ricerca-ateneo	No
University of Padua ¿ Padua, Italy	2014-2016	Clinical utility of plasma-based miRNA signature classifiers in Barrett's carcinogenesis	Collaborator	41139	Fassan Matteo	http://www.unipd.it/ricerca/finanziamenti/finanziamenti-ateneo/progetti-ricerca-ateneo, University of Padua ¿ Padua, Italy	No

* Attached Certification Letter (Y/N)

Certification letter:

Ministero della Salute
Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti
BANDO 2016 PROGETTO COMPLETO

Project Title:
Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests

Project Code:	NET-2016-02363853-7	**Principal Investigator:**	RUGGE Massimo
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Project Type: WP PROJECT - 7

Proposed total budget (Euro)

Costs	TOTAL BUDGET	Co-Funding	Project costs proposed to funding Organization (no moh request)	List of costs proposed for funding to the moh
1 Staff salary	170.268,00	170.268,00	0,00	
2 Researchers contracts	180.000,00	0,00	180.000,00	0,00
3a Equipment (leasing)	150.000,00	0,00	150.000,00	0,00
3b Supplies	120.000,00	0,00	120.000,00	0,00
3c Model costs	0,00	0,00	0,00	0,00
4 Subcontracts	0,00	0,00	0,00	0,00
5 Patient costs	0,00	0,00	0,00	0,00
6 IT services and data bases	22.500,00	0,00	22.500,00	0,00
7 Travels	30.000,00	0,00	30.000,00	0,00
8 Pubblication costs	7.000,00	0,00	7.000,00	0,00
9 Training and Dissemination	31.863,00	0,00	31.863,00	0,00
10 Overheads	54.136,00	0,00	54.136,00	0,00
11 Coordination costs	0,00	0,00	0,00	0,00
Total	765.767,00	170.268,00	595.499,00	0,00

Report the Co-Funding Contributor:
Università degli Studi di Padova

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Ministero della Salute Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti BANDO 2016 PROGETTO COMPLETO		**Project Title:** Monitoring the procedures of the cancer profiling to improve the efficiency of the oncological diagnostic-therapeutic protocols: from the histology phenotyping to the companion diagnostic tests	
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