Fondazione Regionale per la Ricerca Biomedica

DECRETO NR. 130 del 22.11.2024

OGGETTO: BANDO TRANSCAN-3 JOINT TRANSNATIONAL CALL FOR PROPOSALS 2021 - EROGAZIONE RATA IN FAVORE DELL'ISTITUTO EUROPEO DI ONCOLOGIA, PARTNER DEL PROGETTO PIXEL (TRANSCAN3-JTC2021-111) - CUP J47G22000590002.

L'atto si compone di 41 pagine
di cui 35 pagine di allegati

Fondazione Regionale per la Ricerca Biomedica

IL DIRETTORE GENERALE DELLA FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA

PREMESSO CHE:

- l'Istituto Europeo di Oncologia (di seguito "*Beneficiario*"), Partner nr. 4 del progetto dal titolo **"***Profiling and functional analysis of the Immune environment of eXtramedullary leukemia rELapses***",** Acronimo PIXEL (TRANSCAN 2021–111), Responsabile Scientifico Dottor Enrico Derenzini, è risultato ammesso a finanziamento nell'ambito del programma europeo ERA-NET TRANSCAN-3 per un importo complessivo pari a € 200.000,00;
- il Beneficiario ha inviato a FRRB in data 09.08.2022 (PEC Prot. nr. 20220284E) la "*Dichiarazione di svolgimento di attività non economica ai sensi delle norme in materia di aiuti di Stato*" e la "*Dichiarazione di accettazione del contributo*" comunicando successivamente la data di avvio progetto (PEC Prot. nr. 20220384E del 24.10.2022) fissata all'01.11.2022 per una durata di 36 mesi;
- con la DGR n. XI/3476 del 05.08.2020 con la quale è stato approvato il Piano d'Azione 2020 che prevede, al suo interno, l'allocazione fino ad un massimo di euro 1.500.000,00 per la partecipazione di FRRB al bando internazionale TRANSCAN-3 JTC 2021;

CONSIDERATO CHE:

- in data 13.12.2022 il Beneficiario ha firmato la Convenzione relativa al progetto Acronimo PIXEL successivamente controfirmata in data 09.01.2023 dal Direttore Generale di FRRB;
- in data 16.01.2023 (PEC Prot. nr. 20230026E) il Beneficiario ha comunicato la rinuncia all'anticipo;
- l'Articolo 8 della sopracitata Convenzione, stabilisce che l'erogazione al Beneficiario sarà effettuata da FRRB secondo le seguenti modalità:
  - "*…. due tranche successive entro 60 giorni dalla presentazione della prima e della seconda rendicontazione annuale, verificata la correttezza e completezza della documentazione economica e scientifica inviata, e*

calcolate in base ai costi eleggibili effettivamente rendicontati. (…)";

DATO ATTO CHE:

- in data 20.12.2023, è pervenuta dal Beneficiario (PEC Prot. nr. 20230556E) la documentazione economica relativa al primo anno di attività – periodo 01.11.2022-31.10.2023 – del progetto PIXEL, richiesta da FRRB con lettera del 30.10.2023 (PEC Prot. nr. 20230425U);
- in data 22.12.2023, FRRB ha comunicato al Beneficiario (PEC Prot. nr. 20230529U) l'esito positivo dell'istruttoria di verifica della rendicontazione economica pervenuta, richiedendo, al contempo, l'invio della richiesta di erogazione e della dichiarazione sulla ritenuta del 4%;
- il report scientifico del primo anno è stato inviato a FRRB il 12.03.2024;

CONSIDERATO CHE:

- all'art. 8.3 della Convenzione relativa al progetto Acronimo PIXEL si precisa che:
  - *"Nel caso di soggetti privati, l'erogazione del contributo sarà subordinata […] all'ottenimento, per il tramite della Banca Dati Nazionale Antimafia, della documentazione antimafia (solo nel caso di contributi superiori a € 150.000,00) nei modi e nei termini di cui all'Art. 92 D. Lgs. 159/2011 e* successive modifiche;
- in attuazione a tale articolo, FRRB ha presentato, per via telematica tramite la Banca Dati Nazionale Antimafia (BDNA), in relazione al Beneficiario e al progetto PIXEL, la seguente richiesta di informazione antimafia:
  - protocollo nr. PR_MIUTG_Ingresso_0329834_20241017 del 17.10.2024 per l'Istituto Europeo di Oncologia con sede legale in Milano, via Filodrammatici, nr. 10;
  - alla data odierna, trascorso il termine minimo di 30 giorni dall'invio della richiesta di informazione antimafia relativa al soggetto privato lombardo assegnatario di un contributo superiore a € 150.000,00 nell'ambito del progetto europeo PIXEL, FRRB è in attesa del nulla osta da parte della competente Prefettura;
  - ai sensi dell'art. 92 comma 3 del D. Lgs. 159/2011 i contributi, i finanziamenti, le agevolazioni e le altre erogazioni possono essere corrisposti sotto condizione

risolutiva e l'amministrazione interessata può revocare le autorizzazioni e le concessioni o recedere dai contratti, fatto salvo il pagamento del valore delle opere già eseguite ed il rimborso delle spese sostenute per l'esecuzione del rimanente, nei limiti delle utilità conseguite. Le facoltà di revoca e di recesso si applicano anche quando gli elementi relativi a tentativi di infiltrazione mafiosa siano accertati successivamente alla stipula del contratto, alla concessione dei lavori o all'autorizzazione del subcontratto;

PRESO ATTO che il Responsabile dell'Area Amministrativa, Dr. Marco Trincavelli, ha verificato che lo stanziamento di € 2.500,00 è finanziariamente sostenibile al capitolo di spesa 20.15.5033, rientrante nei bandi previsti nel Piano di Azione FRRB relativo all'esercizio 2020, approvato da Regione Lombardia con DGR n. XI/3476 del 05.08.2020 e incassato da FRRB in data 09.11.2020;

VERIFICATA la regolarità contributiva dell'ente assegnatario del contributo – Istituto Europeo di Oncologia – tramite acquisizione d'ufficio del DURC da parte di FRRB;

RICHIAMATI:

- la DGR nr. IX/2401 del 26.10.2011 con la quale è stata istituita la Fondazione Regionale per la Ricerca Biomedica (FRRB);
- la DGR nr. X/5221 del 31.05.2016 con la quale è stato approvato lo Statuto di FRRB, modificato con DGR nr. XI/5786 del 21.12.2021 e con Deliberazione del Consiglio di Amministrazione di FRRB del 26.02.2022;
- la DGR n. XII/1670 del 28.12.2023, con la Giunta ha approvato il nuovo Accordo di cooperazione tra Regione Lombardia e FRRB per lo sviluppo e la valorizzazione di iniziative a favore della ricerca biomedica in Lombardia e della competitività del territorio lombardo nel settore delle Scienze della Vita per il periodo 1° gennaio 2024 – 31 dicembre 2025;
- la DDG n° XII/64 del 27.03.2023 avente ad oggetto: "Determinazioni in ordine alla

Fondazione Regionale per la Ricerca Biomedica

Designazione del Direttore Generale della Fondazione Regionale per la Ricerca Biomedica (Frrb)" e la Deliberazione del Consiglio di Amministrazione di FRRB del 31.03.2023 che ha nominato la Dott.ssa Veronica Comi quale Direttore Generale;

VISTI:

- il Regolamento (UE) nr. 1291/2013 del Parlamento Europeo e del Consiglio dell'11.12.2013 che ha istituito il Programma Quadro per la Ricerca e l'Innovazione 2014-2020 "Horizon 2020" quale strumento di finanziamento della ricerca scientifica e dell'innovazione per progetti di ricerca o azioni volte all'innovazione scientifica e tecnologica che portino un significativo impatto sulla vita dei cittadini europei;
- il Grant Agreement nr. 964264 firmato il 02.02.2021 dalla Commissione Europea e da un partenariato internazionale coordinato dal Ministero della Salute e composto da un totale di 31 enti provenienti da 19 paesi (tra cui Ministeri, funding agencies nazionali e regionali e Consigli di ricerca);
- la Comunicazione della Commissione Europea nr. 2014/C 198/01 "Disciplina degli aiuti di Stato a favore di ricerca, sviluppo e innovazione" e ss.mm.ii.;
- il Regolamento UE nr. 2021/1237 della Commissione del 23.07.2021 che ha modificato il Regolamento UE nr. 651/2014, il quale dichiara alcune categorie di aiuti compatibili con il mercato interno in applicazione degli articoli 107 e 108 del Trattato;

DECRETA

per i motivi espressi in premessa, parte integrante del presente provvedimento:

1. di autorizzare l'erogazione in favore dell'Istituto Europeo di Oncologia, avente sede legale in Milano, via Filodrammatici nr. 10, di un importo pari a € 2.500,00 di cui € 100,00 da versare all'erario a titolo di ritenuta 4% corrispondente alle spese sostenute e considerate eleggibili da FRRB a conclusione delle attività relative alla prima annualità del progetto dal titolo "Profiling and functional analysis of the Immune environment of eXtramedullary leukemia rELapses", Acronimo PIXEL (TRANSCAN 2021–111), Responsabile Scientifico Dr. Enrico Derenzini (CUP J47G22000590002);

Fondazione Regionale per la Ricerca Biomedica

2. di provvedere alla pubblicazione del presente Decreto sul sito web di FRRB, a cura del Responsabile del procedimento ai sensi della Legge 241/1990, Dott.ssa Giulia Maria Rossignolo.

IL DIRETTORE GENERALE
Veronica Comi

Veronica
Comi
22.11.2024
16:36:37
GMT+02:00

COST STATEMENT

Rev.0 del 31/10/2022

EU PROJECT (please select) TRANSCAN 3
JTC ERA-NET TRANSCAN 3 Joint Transnational Call 2021 (JTC 2021)
PROJECT ID TRANSCAN2021-111
PROJECT TITLE AND ACRONYM Profiling and functional analysis of the Immune environment of eXtramedullary leukemia rELapses (PIXEL)
LOMBARDY BENEFICIARY Istituto Europeo di Oncologia
NAME OF PRINCIPAL INVESTIGATOR Enrico Derenzini
CUP NUMBER J47G22000590002
REPORTING PERIOD (FROM-TO) 01/11/2022 - 31/10/2023 YEAR (please select) 1
IS VAT RECOVERABLE? (YES/NO) YES - Partially

COST CATEGORIES	TOTAL BUDGET	REPORTING PERIOD 1	REPORTING PERIOD 2	REPORTING PERIOD 3	TOTAL COST STATEMENT	DEVIATION FROM ORIGINAL BUDGET
TOTAL PERSONNEL COSTS	*€ 75.000,00*	*€ 2.083,33*			€ 2.083,33	€ 72.916,67
CONSUMABLES	*€ 79.500,00*				€ 0,00	€ 79.500,00
EQUIPMENT (LEASING OR ON HIRE)	*€ 0,00*				€ 0,00	€ 0,00
TRAVEL & ACCOMODATION	*€ 5.000,00*				€ 0,00	€ 5.000,00
PUBLICATIONS	*€ 3.000,00*				€ 0,00	€ 3.000,00
OTHER DIRECT COSTS	*€ 0,00*				€ 0,00	€ 0,00
SUBTOTAL	**€ 162.500,00**	**€ 2.083,33**	**€ 0,00**	**€ 0,00**	**€ 2.083,33**	€ 160.416,67
OVERHEADS	*€ 32.500,00*	*€ 416,67*	*€ 0,00*	*€ 0,00*	*€ 416,67*	€ 32.083,33
SUBCONTRACTING COSTS	*€ 5.000,00*	*€ 0,00*	*€ 0,00*	*€ 0,00*	*€ 0,00*	€ 5.000,00
TOTAL REQUESTED BUDGET	**€ 200.000,00**	**€ 2.500,00**	**€ 0,00**	**€ 0,00**	**€ 2.500,00**	**€ 197.500,00**

PERSONNEL COSTS

Please refer to the JTC guidelines for the eligibility of personnel costs

NAME	POSITION	CONTRACT TYPE	PERIOD (FROM - TO)	EURO AMOUNT
Mangione Marta	PhD Student	Fellowship	01/10/2023 - 31/10/2023	2.083,33
			TOTAL € AMOUNT	**2.083,33**

CONSUMABLES

Please refer to the JTC guidelines for the eligibility of costs

NAME	ITEM DESCRIPTION	INVOICE NR.	INVOICE DATE	PAYMENT DATE	EURO AMOUNT
				TOTAL € AMOUNT	0,00

EQUIPMENT (LEASING OR ON HIRE)

NAME	ITEM DESCRIPTION	INVOICE NR.	INVOICE DATE	EURO AMOUNT	% OF USE OF THE EQUIPMENT FOR PROJECT'S PURPOSES	AMORTISATION MONTHS	EURO AMOUNT
						TOTAL € AMOUNT	0,00

TRAVEL AND ACCOMODATION

Max 10% of direct costs

NAME	REASON FOR TRAVELING	DESTINATION	PERIOD (FROM - TO)	EURO AMOUNT
			TOTAL € AMOUNT	0,00

PUBLICATIONS

max 5% of direct costs

NAME	DESCRIPTION	INVOICE NR.	INVOICE DATE	EURO AMOUNT
			TOTAL € AMOUNT	0,00

OTHER DIRECT COSTS

Please refer to the JTC guidelines for the eligibility of costs

NAME	ITEM DESCRIPTION	INVOICE NR.	INVOICE DATE	PAYMENT DATE	EURO AMOUNT
				TOTAL € AMOUNT	0,00

SUBCONTRACTING

Max 20% of direct costs

NAME	PROCEDURE APPLIED	DESCRIPTION (provide details on service duration)	INVOICE NR.	INVOICE DATE	EURO AMOUNT
				TOTAL € AMOUNT	0,00

I declare that all the documentation listed in this table is archived at the Beneficiary premises and available in case of financial audits.

Name of the Beneficiary Legal Representative
Mauro Melis

Signature of the Beneficiary Legal Representative

Firmato da:
MAURO MELIS
Codice fiscale: MLSMRA55B09A271I
Organizzazione: NON PRESENTE
Valido da: 04-05-2021 09:34:54 a: 04-05-2024 01:00:00
Certificato emesso da: InfoCert Qualified Electronic Signature CA 3, InfoCert S.p.A., IT
Riferimento temporale 'SigningTime': 14-12-2023 13:27:58
Motivo: Approvo il documento

Date, Place
14/12/2023, Milan

IEO
Istituto Europeo di Oncologia
Istituto di Ricovero e Cura a Carattere Scientifico
Via Ripamonti 435 20141 Milano
T +39 02 57489.1 F +39 02 57489.208
W www.ieo.it

RICHIESTA EROGAZIONE CONTRIBUTO

DICHIARAZIONE SOSTITUTIVA DI ATTO NOTORIO
(D.P.R. 445/2000)

Spett.le
Fondazione Regionale
per la Ricerca Biomedica
Via T. Taramelli, 12
20124 Milano

PEC:
fondazioneregionalericercabiomedica@pec.it

OGGETTO: Richiesta erogazione contributo - prima tranche

TITOLO PROGETTO: "Profiling and functional analysis of the Immune environment of eXtramedullary leukemia rELapses (PIXEL)"

RESPONSABILE SCIENTIFICO: Dottor Enrico Derenzini

CODICE CUP: J47G22000590002

Il sottoscritto Mauro Melis, nato ad _____

domiciliato per la carica in Milano (MI) - CAP 20121 - Via Filodrammatici n.10

in qualità di Legale Rappresentante dell'Ente Istituto Europeo di Oncologia, partecipante al progetto in oggetto

con sede legale in Milano (MI) - CAP 20121 - Via Filodrammatici n. 10

Codice Fiscale / P.IVA 08691440153

Indirizzo email: grantsofficeieo@pec.it; servizio.grantsoffice@ieo.it

CHIEDE

l'erogazione della prima rata pari a € 2.500,00

IEO
Istituto Europeo di Oncologia
Istituto di Ricovero e Cura a Carattere Scientifico
Via Ripamonti 435 20141 Milano
T +39 02 57489.1 F +39 02 57489.208
W www.ieo.it

Le coordinate per il versamento sono le seguenti:

- Banca: Banca Popolare di Sondrio
- Agenzia: Sede di Milano
- IBAN: IT66 F056 9601 6000 0000 9429 X53

Cordiali saluti,

Milano, 02/01/2024

F.to DIGITALMENTE
DAL LEGALE RAPPRESENTANTE
(*o suo delegato, ai sensi dell'Art. 24 del DLgs n. 82/2005*)

Firmato da:
MAURO MELIS
Codice fiscale: MLSMRA55B09A271I
Organizzazione: NON PRESENTE
Valido da: 04-05-2021 09:34:54 a: 04-05-2024 01:00:00
Certificato emesso da: InfoCert Qualified Electronic Signature CA 3, InfoCert S.p.A., IT
Riferimento temporale 'SigningTime': 02-01-2024 16:17:05
Motivo: Approvo il documento

IEO
Istituto Europeo di Oncologia
Istituto di Ricovero e Cura a Carattere Scientifico
Via Ripamonti 435 20141 Milano
T +39 02 57489.1 F +39 02 57489.208
W www.ieo.it

MODELLO DICHIARAZIONE RITENUTA 4%*

Il Sottoscritto Mauro Melis,
nato a
il

in qualità di rappresentante legale dell'ente
Istituto Europeo di Oncologia

P. IVA / Cod. Fiscale 08691440153

domiciliato per la carica
in Via Filodrammatici n. 10 Milano

consapevole che le dichiarazioni mendaci sono punite penalmente ai sensi dell'art. 76 del D.P.R. 28 dicembre 2000, n. 445, e che codesta Amministrazione effettuerà controlli, anche a campione, sulle dichiarazioni rese

DICHIARA

che, ai fini dell'applicazione della ritenuta del 4% prevista dal secondo comma dell'art. 28 del D.P.R. 29 settembre 1973, n. 600, il contributo oggetto della richiesta a cui viene allegata la presente dichiarazione è da considerarsi come segue: (1)

SOLO PER ENTI COMMERCIALI

X L'ente beneficiario svolge attività commerciale in via esclusiva o principale; **(soggetto a ritenuta)**

SOLO PER ENTI NON COMMERCIALI

☐ L'ente beneficiario, pur non svolgendo attività commerciale in via esclusiva o principale, destina il contributo alla riduzione di oneri gestionali o alla copertura di disavanzi di gestione cui concorrono entrate derivanti da attività di natura commerciale; **(soggetto a ritenuta; nel caso di quota di finanziamento/cofinanziamento U.E., tale quota non è soggetta a ritenuta)**

☐ Il contributo è destinato unicamente alla copertura di spese o di disavanzi alla cui formazione concorrono solo entrate di carattere istituzionale; (2) **(non soggetto a ritenuta)**

☐ L'ente beneficiario è un'organizzazione non lucrativa di utilità sociale – ONLUS – (organizzazione iscritta nel registro provinciale di volontariato, cooperativa sociale, ecc., di cui all'art. 10, D. Lgs. n. 460/97); (3) **(non soggetto a ritenuta)**

IEO
Istituto Europeo di Oncologia
Istituto di Ricovero e Cura a Carattere Scientifico
Via Ripamonti 435 20141 Milano
T +39 02 57489.1 F +39 02 57489.208
W www.ieo.it

IN GENERALE

☐ Il contributo viene dichiarato esente dalla ritenuta medesima in virtù di un'espressa deroga ai *sensi della legge* _____*;* (4) **(non soggetto a ritenuta)**

Il sottoscritto **dichiara**, altresì, che provvederà a comunicare tempestivamente eventuali variazioni che dovessero intervenire a modificare la presente dichiarazione, ivi comprese, in particolare, quelle previste dall'art. 149 del D.P.R. 22 dicembre 1986, n. 917 (in rif. alla perdita della qualifica di ente non commerciale).

Milano, 02/01/2024 Firma

Firmato da:
MAURO MELIS
Codice fiscale: MLSMRA55B09A271I
Organizzazione: NON PRESENTE
Valido da: 04-05-2021 09:34:54 a: 04-05-2024 01:00:00
Certificato emesso da: InfoCert Qualified Electronic Signature CA 3, InfoCert S.p.A., IT
Riferimento temporale 'SigningTime': 02-01-2024 16:17:42
Motivo: Approvo il documento

***Allegare fotocopia della Carta di Identità o di un documento equipollente.**

(1) apporre una crocetta sul punto interessato
(2) rif. art. 143, comma 1 D.P.R. 22 dicembre 1986, n. 917; le entrate derivano esclusivamente da contributi dei soci o degli Enti Pubblici e comunque, anche nel caso in cui ci fossero entrate di altro genere di natura commerciale, queste ultime vengono gestite con contabilità separata rispetto a quella istituzionale per la quale si richiede il contributo (art. 144, co. 2 D.P.R. 917/86)
(3) rif. art. 16 D.Lgs 460/97.
(4) indicare gli estremi della disposizione normativa.

IEO
Istituto Europeo di Oncologia
Istituto di Ricovero e Cura a Carattere Scientifico
Via Ripamonti 435 20141 Milano
T +39 02 57489.1 F +39 02 57489.208
W www.ieo.it

INFORMATIVA IN MATERIA DI TRATTAMENTO DEI DATI PERSONALI
ai sensi degli artt. 13 e 14 del Regolamento (UE) 2016/679 (GDPR)
"Modulo raccolta dati Dichiarazione Ritenuta 4%"

INFORMATIVA SULLA PRIVACY

1. **Titolare del trattamento e DPO** Titolare del trattamento dei dati personali è la Fondazione Regionale per la Ricerca Biomedica, avente sede legale in Milano, Piazza Città di Lombardia nr. 1 con sedi operative in Milano, Via Torquato Taramelli nr. 12 e in Bruxelles (BE), Casa della Lombardia nr. 2, Place du Champ de Mars - Tel. 02/67650166, e-mail info@frrb.it, PEC fondazioneregionalericercabiomedica@pec.it, sito web www.frrb.it.
Al fine di meglio tutelare gli Interessati, nonché in ossequio al dettato normativo, il Titolare ha nominato un proprio DPO, Data Protection Officer (nella traduzione italiana "RPD, Responsabile della protezione dei dati personali") nella figura del Dottor Ivano Pecis, contattabile scrivendo alla mail privacy@frrb.it o alla PEC dpo.frrb@pec.it.
2. **Finalità, Basi giuridiche e tipologia di Dati trattati** FRRB tratta i dati personali esclusivamente per le finalità e in ragione delle basi giuridiche di seguito indicate: i dati personali da Lei forniti sono necessari per gli adempimenti previsti per legge ed in particolare al fine garantire il trattamento dei dati presenti e previsti nel modello "Dichiarazione ritenuta 4%".
3. **Autorizzati e Responsabili del trattamento** I dati personali sono trattati da personale dipendente di FRRB, previamente autorizzato al trattamento e appositamente istruito e formato. I dati personali possono essere trattati anche da soggetti esterni, formalmente nominati dal Titolare del Trattamento quali Responsabili del trattamento ai sensi dell'art. 28 GDPR, appartenenti alle seguenti categorie: società che erogano servizi tecnico/informatici; società che erogano servizi di comunicazioni telematiche e, in particolar modo, di posta elettronica; società che erogano servizi di gestione e conservazione documentale; soggetti cui la FRRB ha affidato lo svolgimento dell'istruttoria di ammissibilità/ricevibilità della domanda.
4. **Destinatari e Pubblicazione dei dati personali** I dati personali degli Interessati potranno essere comunicati ad altri soggetti che trattano i dati in qualità di Titolari autonomi del trattamento: potranno essere comunicati al personale interno della Fondazione o a consulenti esterni debitamente istruiti dal Titolare. in caso di contenzioso, all'Autorità giudiziaria e ai legali del Titolare.
5. **Natura del conferimento dei dati** Il conferimento dei dati richiesti è necessario. Il mancato conferimento (totale o parziale) non consente il corretto prosieguo dell'iter amministrativo di valutazione ed eventuale accoglimento della dichiarazione.
6. **Periodo di conservazione dei dati** I dati personali degli Interessati vengono conservati dalla Fondazione per un periodo di tempo massimo di 10 anni dalla data di sottoscrizione della dichiarazione, fatta salva la necessità di prolungare la conservazione dei dati sino alla definizione di eventuali contenziosi, ovvero sino alla conclusione di eventuali attività di vigilanza e controllo operate da Enti terzi.
7. **Trasferimento dei dati in Paesi extra-SEE** FRRB può avvalersi, anche per il tramite dei propri Responsabili del trattamento, di società di servizi di comunicazione telematica e, in particolar modo, di posta elettronica, che potrebbero collocare o far transitare i messaggi e le informazioni personali degli utenti anche in Paesi non appartenenti allo Spazio Economico Europeo (SEE) o che in tali Paesi potrebbero salvare copie di backup dei dati. Al fine di garantire un adeguato livello di protezione dei dati personali, queste società possono attuare il trasferimento solo verso Paesi (o settori di questi) che sono stati oggetto di apposite decisioni di adeguatezza adottate dalla Commissione europea, oppure sulla base di Clausole Contrattuali Standard approvate dalla Commissione stessa.
8. **Diritti dell'Interessato** Il Regolamento (UE) 2016/679 riconosce agli Interessati diversi diritti esercitabili contattando il Titolare o il DPO ai recapiti indicati al punto 1 della presente informativa. Tra i diritti esercitabili, purché ne ricorrano i presupposti di volta in volta previsti dalla normativa (in particolare, artt. 15 e seguenti del Regolamento) vi sono: il diritto di conoscere se la Fondazione ha in corso trattamenti di dati personali che riguardano l'Interessato e, in tal caso, di avere accesso ai dati oggetto del trattamento e alle informazioni a questo relative; il diritto alla rettifica dei dati personali inesatti che riguardano l'interessato e/o all'integrazione di quelli incompleti; il diritto alla cancellazione dei dati personali che riguardano l'interessato; il diritto alla limitazione del trattamento; il diritto di opporsi al trattamento; il diritto alla portabilità dei dati personali; il diritto di revocare il consenso in qualsiasi

IEO
Istituto Europeo di Oncologia
Istituto di Ricovero e Cura a Carattere Scientifico
Via Ripamonti 435 20141 Milano
T +39 02 57489.1 F +39 02 57489.208
W www.ieo.it

momento, senza che ciò pregiudichi la liceità del trattamento, basato sul consenso, effettuato prima della revoca. Per ricevere maggiori informazioni sui diritti esercitabili, ciascun Interessato può rivolgersi direttamente al Titolare o al DPO. In ogni caso, l'Interessato ha anche il diritto di presentare un formale Reclamo all'Autorità garante per la protezione dei dati personali, secondo le modalità reperibili sul sito internet www.garanteprivacy.it

Durc On Line

Numero Protocollo	INAIL_46005365	Data richiesta	16/10/2024	Scadenza validità	13/02/2025

Denominazione/ragione sociale	ISTITUTO EUROPEO DI ONCOLOGIA SRL
Codice fiscale	08691440153
Sede legale	VIA FILODRAMMATICI, 10 20121 MILANO (MI)

Con il presente Documento si dichiara che il soggetto sopra identificato RISULTA REGOLARE nei confronti di

I.N.P.S.

I.N.A.I.L.

Il Documento ha validità di 120 giorni dalla data della richiesta e si riferisce alla risultanza, alla stessa data, dell'interrogazione degli archivi dell'INPS, dell'INAIL e della CNCE per le imprese che svolgono attività dell'edilizia.

TRANSCAN Call 2021

Periodic Report

Project Information

Project number TRANSCAN-2021-111-PIXEL

Project acronym PIXEL

Project title Profiling and functional analysis of the Immune environment of eXtramedullary leukemia rELapses

Project proposal *

transcan2021-111_project_description_PIXEL.pdf
(24/02/2024, 4970.39 kb)

Project duration (months) 36 months

Project starting date 01/11/2022

Consortium Agreement signed (date) 08/01/2024

Total budget of the project (EUR) 1.525.432,39

Period covered by this report 01/11/2022 - 31/10/2023

Periodic report no. 1st

Date of submission of the periodic report 08th of March, 2024

Project website (if any)

Project social media (if any)

Name of the Coordinator Luca Aldo Edoardo Vago

Email of the Coordinator vago.luca@hsr.it

Consortium composition

1. Project Coordinator (P1)

Organisation details	Principal Investigator (PI - Project Leader)
Organisation country Italy	**First name** Luca Aldo Edoardo
Organisation region (IF APPLICABLE)	**Last name** Vago
Organisation name IRCCS Ospedale San Raffaele	**Gender** Male
Type of organisation Clinical/hospital/health organisation	**Involved in WPs** 1-2
Type of sector	**Project funding organisations**

Public-Private

Fondazione Regionale per la Ricerca Biomedica (FRRB)

2. Partner 2 (P2)

Organisation details	Principal Investigator (PI - P2)
Organisation country Germany	**First name** Robert
Organisation region (IF APPLICABLE)	**Last name** Zeiser
Organisation name Universitätsklinikum Freiburg	**Gender** Male
Type of organisation Clinical/hospital/health organisation	**Involved in WPs** 1-2
Type of sector Public	**Project funding organisations** Federal Ministry of Education and Research (BMBF)

3. Partner 3 (P3)

Organisation details	Principal Investigator (PI - P3)
Organisation country Germany	**First name** Friedrich
Organisation region (IF APPLICABLE)	**Last name** Stölzel
Organisation name UKSH Universitätsklinikum Schleswig-Holstein	**Gender** Male
Type of organisation Clinical/hospital/health organisation	**Involved in WPs** 1-2
Type of sector Public	**Project funding organisations** Federal Ministry of Education and Research (BMBF)

4. Partner 4 (P4)

Organisation details	Principal Investigator (PI - P4)
Organisation country Italy	**First name** Enrico
Organisation region (IF APPLICABLE)	**Last name** Derenzini
Organisation name	

IRCCS Istituto Europeo di Oncologia (IEO)

Type of organisation
Clinical/hospital/health organisation

Type of sector
Public

Gender
Male

Involved in WPs
1-2

Project funding organisations
Fondazione Regionale per la Ricerca Biomedica (FRRB)

5. Partner 5 (P5)

Organisation details	Principal Investigator (PI - P5)
Organisation country Austria	**First name** Armin
Organisation region (IF APPLICABLE)	**Last name** Zebisch
Organisation name Medical University of Graz	**Gender** Male
Type of organisation Clinical/hospital/health organisation	**Involved in WPs** 1-2
Type of sector Public	**Project funding organisations** Austrian Science Fund (FWF)

6. Partner 6 (P6)

Organisation details	Principal Investigator (PI - P6)
Organisation country Spain	**First name** Maria Carolina
Organisation region (IF APPLICABLE)	**Last name** Florian
Organisation name Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL)	**Gender** Female
Type of organisation Research organisation	**Involved in WPs** 1-2
Type of sector Public	**Project funding organisations** Fundación Científica de la Asociación Española contra el Cáncer (FCAECC); Instituto de Salud Carlos III (ISCIII)

Consortium details

Has there been any change in the consortium composition since the start of the project?

No

Previous experience in working together within the consortium

(select the appropriate option) Yes, with part of the consortium

If yes, please indicate which partner(s) collaborated previously (partner number)

- P01, P02 and P03 have already collaborated and have a clear record of high-impact collaborative papers;
- P01 and P02 have also ongoing collaboration studies apart from the present proposal;
- P03 and P04 have a clear record of high-impact collaborative papers

Progress Report

Summary of Progress against Objectives

Describe the work performed during the period and assess it with respect to the initial work plan.
- Summary of the project and objectives included in the initial research proposal
- Main results, in particular highlighting the main scientific/technical achievements of the project, its contribution to the State of the Art and its impact
- Conclusions

Acute myeloid Leukaemia (AML) relapses after allogeneic hematopoietic cell transplantation (allo-HCT) are mainly driven by the evasion of leukemic cells from the donor derived immune system, unable to control residual leukemic cells. Some relapses after allo-HCT may occur in the extramedullary (EM) sites, suggesting a causative link between altered tissue homing and immune escape, and exemplifying how the microenvironment can impact on the efficacy of adoptive immunotherapy.
In the present project we will leverage on the complementary clinical and translational expertise of the six partners to study in unprecedented detail the immunobiology of extramedullary (EM) posttransplantation AML relapses, and in particular:
- we will combine the latest omic technologies to "pixelize" EM relapses into their finest details to characterize the relative contributions of tumor-intrinsic features, immune system and non-immune microenvironment in the origin and maintenance of EM relapses, comparing them with BM samples at diagnosis and after allo-HCT;
- and then, we will reconstruct and validate their driver processes through advanced ex vivo functional assays and in vivo animal modeling to identify and functionally validate new molecular drivers of EM relapses, ultimately to exploit them as vulnerabilities for targeted therapeutic approaches.

WP1: Integrative multiomic and functional profiling of the biological mechanisms at the basis of EM AML relapse.
All the technologies and assays proposed to detail the multiomic and functional profiling of EM diseases base their feasibility on the pre-processing steps, that lead from the whole EM tissue, recovered from patient or mice, to single cell suspensions viable or not, or to thin thick tissue slides, according to the downstream assay that should be performed.
In general, the Consortium composed by all the partners was able set up the protocols to isolate a single cell suspension for both nucleic acid extraction (for exome sequencing, RNAseq and scATACseq) and functional experiments (for in vitro immunological assays and for the infusion in in vivo mouse models). Moreover, the Consortium set up the pre-staining and pre-detection procedures to generate 3-4 µm thick EM tissue sections, both from formaldehyde-fixed paraffin-embedded (FFPE) or cryo-preserved tissue blocks, for spatial transcriptome and high-content histopathological analyses.
Based on these pre-processing steps that were tuned and implemented among and between all the partners of the Consortium, first feasibility tests were performed on EM samples already in loco available for each partner.

Optimization of high-throughput profiling technologies to analyse and compare EM and BM primary leukemia samples.
The set-up of the different high-throughput profiling technologies (exome sequencing, spatial transcriptomics, scATACseq, high-content histopathology, kinase signalling mapping, metabolic fingerprinting) was carried out in order to detail a multimodal map of the EM diseases.
In particular, P03 and P05 have already optimized the genomic extraction from FFPE and fresh/frozen EM samples and tested the feasibility to perform whole exome sequencing (WES). In addition to the original project, P05 have already validated on FFPE EM samples a targeted sequencing panel, covering more than 40 genes recurrently mutated in myeloid neoplasms and tested in more than 30 primary patient specimens of EM leukemia samples, and where possible of the corresponding BM aspirates collected simultaneously. This myeloid panel is now under implementation in order to reach the sequencing of more than 300 genes. Both the WES and target panel datasets will benefit from the low coverage whole exome sequencing of the patient germline for the definition of the somatic variants that will be used for clonal deconvolution studies. Moreover, in order to define the clonal and subclonal hierarchy and trajectories of EM AML, the genomic results here obtained will be compared to WES datasets of BM AML at diagnosis, at relapse after conventional therapy and after allo-HCT in other patients (available to P01 and P03 through a previous collaborative project), and when possible from the same patient. P04 had optimized a Nanostring nCounter® PanCancer Immune Profiling Panel (Cesano, J Immunother Cancer, 2015), a unique 770-plex gene expression panel to measure the human immune responses, providing single cell and spatial information on both FFPE and cryo-preserved EM samples. With this technology P04 has, so far, already tested 8 EM samples. The quality check analyses, performed according to Nanostring requirements, have highlighted a good quality of the analyzed samples, resulting in high quality data. Then, data obtained by spatial transcriptomics will be compared with the scRNAseq dataset already available to P01 for BM relapses, and generated by P03 from the processing of collected EM relapses. P06 has fully optimized the “Simultaneous high-throughput ATAC and RNA expression with sequencing” (SHARE-seq)” protocol (Ma et al., Cell, 2020) on BM aspirates. In the next months from the same patients the profile of BM aspirates and EM tissues biopsies from leukemia patients will be performed. By preliminary sequencing studies, P05 has proved that RAS mutations are particularly frequent in EM samples. Then, the assessment of the pathological role of

other kinase signaling genes and pathways is ongoing, taking advantage of the phospho-flow and phosphotyrosine kinase (PTK) and serine-threonine kinase (STK) PamChip arrays. The institution of the Project Coordinator has recently acquired the Phenocycler Fusion platform from Akoya Bioscience, that is an integrated multiplex immunofluorescence platform, that utilize proprietary antibodies with a molecular barcode system for marker detection. During this first year grant, on the basis of prior knowledge on the cells and structure involved in the cross-talk between leukemia and non-leukemia microenvironment a panel of 46 different intra- and extra-cellular markers was optimized, that will be tested on both EM tissue samples and on BM core biopsies. The first tests revealed the feasibility to analyze both FFPE and frozen EM slides, and also FFPE Bouin-decalcified BM tissue samples. In addition, the Phenocycler Fusion platform, in the case of need and in parallel to the high-content immunopathology analysis, will allow us to implement also the spatial transcriptomic on the same EM tissue sample. Finally, P02 has already optimized the analysis of the metabolic status of both leukemia and immune cells from bone marrow aspirates, as documented in a previous publication (Uhl, Sci Transl Med. 2020). Taking advantage of the protocols already established by the Consortium for EM tissue disaggregation, the metabolic status of tumor and non-tumor immune cells recovered from EM samples will be easily tested in the upcoming months.
It should be stressed that, especially, for some omic technologies (like SHARE-seq, PamChip arrays and metabolic status analysis), sample availability and quality are relevant issues. So, the complete feasibility of these tasks will be provided once EM samples from other centers will be analysed, taking advantage of the collaborative network generated as main objective of the WP2.

Setup/finetuning of in vitro and in vivo tools to test and compare the functional behaviour of EM and BM primary samples.
In the second part of this work package, we aim at delineating the functional relevance of genomic, transcriptomic and metabolic changes by employing state-of-the-art functional assays on leukemic cell lines and primary EM patient specimens. As written in the incipit of the this scientific section, the main hurdle for the application of the following techniques is to obtain sufficient viable material to perform the functional evaluations, in particular for EM primary samples. This WP will benefit from the pre-processing procedures collaboratively generated by the Consortium, taking advantage of the single expertise of each partner and to the collaborative network generated as goal of WP2.
Preliminary experiments were made by P01 and P02 starting from soft tissues and/or EM localizations recovered from in vivo mouse models. Homogenization and digestion steps are needed to obtain viable and single cell suspension to be used in already optimized immunological, tissue migration/invasion and chemosensitivity assays. Based on the results of the first part of the WP1, P05 has started to analyze the role of RAS mutations. So, by employing CRISPR/Cas9 knock-in technology P05 has created a leukemic cell line models carrying RAS mutations. In vitro migration/invasion assays, it was observed that RAS-mutated cells had an increased migration and invasion potential compared to the RAS-wildtype control cells. Moreover, these results were corroborated in preliminary experiments in the ex ovo CAM assay, where the RAS-mutated cells were able to invade the chorioallantoic membrane and to form large myeloid sarcomas-like masses. Additionally, taking advance of the expertise of P02 a murine xenograft model will be established, where edited leukemia cells will be subcutaneously injected to assess whether the RAS-mutated cells perform better in forming tumors at EM sites. This model will also allow us to delineate whether the leukemic cells are able to leave the EM sites by taking advantage of their migration and invasion abilities.
If all these techniques clearly suffer from sample quality, linked to cell viability, sample abundance is another relevant issue. So, the complete achievability of all these experiments will vary among different primary samples and will be evaluated during the next year once the EM samples collected will circulate within the Consortium, as part of the objectives of WP2.

WP2: Generation of an international collaborative network for the accrual of clinical information, the collection of biological samples and the conduction of interventional studies on EM AML relapses.
As featured in the original project, P01 redacted and circulated an agreement that was then approved and signed by each partner for the generation of a Consortium, that will ease the sharing of the EM and BM tissue samples and of the data generated by each research laboratory, to ultimately easily bring back the impactful results to the clinical practice.
Following this path, the Consortium has already generated a common database, discussed and implemented by all the partners, to collect information on patients enrolled by each partner site. The related spreadsheet comprises some demographic, disease and transplant-related information, that will be relevant for association studies with EM diseases and the possible differences in the surrounding microenvironment between medullary and extramedullary leukemia cells. Moreover, each partner have already got in touch with their institutional or national leukemia groups with a biobanking activity, to finalize an updated list of fresh/frozen and FFPE samples available for medullary and extramedullary AML diseases. Thus, this WP will favor also the circulation of the rare and precious EM tissue samples, to ultimately finalize this challenging project. In fact, as initially proposed the most abundant and good quality samples will be shared among the Consortium to finalize the “multiomic” and “functional” map of EM AML relapses, as described in WP1.
Finally, the Coordinator, in collaboration with his institutional project coordination office, is implementing a platform for the secure, easy transfer and sharing of the wet-lab generated data and of the clinical variables collected.

So, in conclusion for WP1 the Consortium has almost completed the optimization of the pre-processing steps on both fresh/frozen and FFPE preserved EM tissue samples, that are fundamental for the implementation of the multiomic techniques and functional assays.
The complementary information that the techniques originally proposed have and the collaborative work organized among the different partners guarantees that, even if not all the assay proposed will be feasible (for material abundance and quality constrains), a comprehensive map of the EM diseases will be still generated. All these information will be next compared with BM AML samples collected at different stage of the disease from other patients (obtained from retrospective studies from the different partners) and where possible also from the same patients, enrolled for this project, with an EM localization.
Indeed, the already created Consortium, as task of WP2, is allowing from its early beginning to ease data sharing, and will for sure to allow the circulation of primary EM sample and clinical and wet-lab generated data, to ultimately reach the final purposes of the present project.

Publishable summary

Please provide a brief summary of the project in layman's terms(maximum one page). We inform you that the lay summary may be published on the TRANSCAN-3 website, newsletters, etc.

Disease recurrence after allogeneic hematopoietic cell transplantation (allo-HCT) is frequently driven by failure of the donor immune system at controlling the outgrowth of residual cancer cells. Intriguingly, acute myeloid leukemia (AML) relapses after allo-HCT often occur in extramedullary (EM) sites, suggesting a causative link between altered tissue homing and immune escape, and exemplifying how the microenvironment can impact on the efficacy of adoptive immunotherapy.
In the present project, a transnational consortium will investigate the mechanisms driving EM AML relapses, leveraging on the key positioning of

the six partners in national networks to accrue a sizable cohort of cases, and taking advantage of their consolidated and complementary expertise in the use of cutting-edge methodologies to study primary patient samples.
In particular, we will combine the latest omic technologies to "pixelize" EM relapses into their finest details, and then reconstruct and validate their driver processes through advanced ex vivo functional assays and in vivo animal modeling.
Availability of samples collected longitudinally in time will provide the unique controls represented by the same tumor in its microenvironment of origin and before exposure to the immune selective pressure of allo-HCT, allowing to identify features that are unique to EM post-transplantation relapses, and to functionally validate their causative role.
Ultimate goal of the project will be to understand which of the distinctive features of EM relapses is necessary for their emergence and maintenance, and could thus represent a vulnerability to be exploited for targeted therapeutic approaches.

Deviations

Describe any deviations or nature of the difficulties encountered (e.g., technical deadlock, service provider default, failure to meet deadlines, etc); the proposed corrective actions; and, any foreseen need for a contractual project content revision or duration extension.

At least for some of the proposed techniques and assays, there are technical hurdles mainly related to sample size/abundance and quality. So, as written in the “Scientific Section”, the complete achievability of all the “multiomic” and “functional” techniques will be evaluated during the next year, once the EM samples collected will circulate within the Consortium. However, in the case need the Consortium is discussing and evaluating the possibility to study human EM AML harvested, as FFPE or fresh/frozen tissue blocks, from immunodeficient mice after immune pressure, already available in the lab of P01. The implementation of the study of these EM samples will allow us not only to define possible genomic and transcriptomic alterations associated to EM diseases, but also to potentially have a “humanized xenograft model” to functionally assess the role of determinants involved in the acquired migration and invasion abilities of AML cells with an extramedullary localization.

Objectives achievement

The project has achieved most of its objectives and technical goals for the period with relatively minor deviations

How much of the total amount of the work plan has been performed?

Please fill in the table below, add/suppress lines as necessary.

1	**Project as a whole**	[-] 0-20%	[X] 21-40%	[-] 41-60%	[-] 61-80%	[-] 81-100%
2	WP 1	[X] 0-20%	[-] 21-40%	[-] 41-60%	[-] 61-80%	[-] 81-100%
3	WP 2	[-] 0-20%	[X] 21-40%	[-] 41-60%	[-] 61-80%	[-] 81-100%

High-resolution figures

High-resolution figures must be uploaded. The format for figure submission is jpg/tiff

Milestones

Please include the complete list of the milestones of the project, including those due for the last reporting period, if applicable.

Record N° 1

Work Package Number

1

Partners involved

IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
IRCCS Istituto Europeo di Oncologia (IEO) (P4)

Milestones

Optimization of high-throughput profiling technologies (exome sequencing, spatial transcriptomics, scATACseq, high-content histopathology, kinase signalling mapping, metabolic fingerprinting) to analyze and compare EM and BM primary samples

Medical University of Graz (P5)
Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6)

Due month
12

Completed
Yes

Record N° 2

Work Package Number
1

Milestones
Setup/finetuning of in vitro and in vivo tools to test and compare the functional behaviour of EM and BM primary samples (chemosensitivity and invasion/migration assays, murine models)

Partners involved
IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
Medical University of Graz (P5)

Due month
12

Completed
Not yet

Description of the progress for delayed milestones
Please explain the reasons for non-completion and the impact on achieving the overall objectives of the project. Description should not be more than ½ page for each deliverable.

The activation of the grant from the different National funding agencies related to each partner was not aligned for all the partners. Even if this had not an impact on the optimization steps of the WP1, but mainly on the distribution of primary EM and BM samples amongst partners, as sub-task of WP2. However, the complete achievability of all the multiomic and functional experiments, already set up on in loco available material, could vary among primary samples and so could evaluated only once also the EM samples from other centers will be available and circulate within the Consortium.

Record N° 3

Work Package Number
2

Milestones
Generation of a shared database collecting the clinical information of EM relapse cases available to the proponents and to their national reference networks

Partners involved
IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
IRCCS Istituto Europeo di Oncologia (IEO) (P4)
Medical University of Graz (P5)
Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6)

Due month
12

Completed
Yes

Record N° 4

Work Package Number

2

Milestones

Collection and distribution of primary samples amongst partners

Partners involved

IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
IRCCS Istituto Europeo di Oncologia (IEO) (P4)
Medical University of Graz (P5)
Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6)

Due month

12

Completed

Not yet

Description of the progress for delayed milestones

Please explain the reasons for non-completion and the impact on achieving the overall objectives of the project. Description should not be more than ½ page for each deliverable.

The delay in this milestone is mainly related to the distribution of primary samples on which different technologies, already set up from the different partners, should be applied. As mentioned in the “Scientific Information” section each partner has already contacted the institutional and National AML study groups to have access to primary FFPE and/or cryo-preserved EM AML samples. So, each partner have already identified a list of suitable EM samples, part of which are also paired with the corresponding BM disease. As, most of multiomics and functional techniques had completed the optimization step starting, from the next month we will be able start the analysis of EM tissue samples. Indeed, EM samples with sufficient and good quality material will be shared among the different partners to complete the analytical an processing/feasibility steps.

Record N° 5

Work Package Number

1

Milestones

Analysis of the primary EM and BM samples by the profiling technologies, identification of features that are characteristic of EM relapses

Partners involved

IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
IRCCS Istituto Europeo di Oncologia (IEO) (P4)
Medical University of Graz (P5)
Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6)

Due month

24

Completed

Not yet

Description of the progress for delayed milestones

Please explain the reasons for non-completion and the impact on achieving the overall objectives of the project. Description should not be more than ½ page for each deliverable.

To be completed during the second year of the project

Record N° 6

Work Package Number
1

Milestones
Functional testing of primary samples, optimization of conditions to artificially modify selected features in primary samples

Partners involved
IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
Medical University of Graz (P5)

Due month
24

Completed
Not yet

Description of the progress for delayed milestones
Please explain the reasons for non-completion and the impact on achieving the overall objectives of the project. Description should not be more than ½ page for each deliverable.

To be completed during the second year of the project

Record N° 7

Work Package Number
2

Milestones
Integration in the database of biological information, data analysis to identify significant associations between biological data and clinical behaviour

Partners involved
IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
IRCCS Istituto Europeo di Oncologia (IEO) (P4)
Medical University of Graz (P5)
Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6)

Due month
24

Completed
Not yet

Description of the progress for delayed milestones
Please explain the reasons for non-completion and the impact on achieving the overall objectives of the project. Description should not be more than ½ page for each deliverable.

To be completed during the second year of the project

Record N° 8

Work Package Number
1

Milestones
Integration of the data derived from single high-throughput technologies to reconstruct dependencies and model mechanisms of relapse

Partners involved

IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
IRCCS Istituto Europeo di Oncologia (IEO) (P4)
Medical University of Graz (P5)
Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6)

Due month

36

Completed

Not yet

Description of the progress for delayed milestones

Please explain the reasons for non-completion and the impact on achieving the overall objectives of the project. Description should not be more than ½ page for each deliverable.

To be completed during the third year of the project

Record N° 9

Work Package Number

1

Milestones

Validation of the most promising candidate drivers of EM relapse in an independent sample set and through functional in vitro and in vivo assays using artificially modified leukemia cells

Partners involved

IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
Medical University of Graz (P5)

Due month

36

Completed

Not yet

Description of the progress for delayed milestones

Please explain the reasons for non-completion and the impact on achieving the overall objectives of the project. Description should not be more than ½ page for each deliverable.

To be completed during the third year of the project

Record N° 10

Work Package Number

2

Milestones

Elaboration of a multicentric clinical trial proposal to translate findings from the project in novel diagnostic or therapeutic approaches

Partners involved

IRCCS Ospedale San Raffaele (P1)
Universitätsklinikum Freiburg (P2)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
IRCCS Istituto Europeo di Oncologia (IEO) (P4)
Medical University of Graz (P5)
Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6)

Due month

36

Completed

Not yet

Description of the progress for delayed milestones

Please explain the reasons for non-completion and the impact on achieving the overall objectives of the project. Description should not be more than ½ page for each deliverable.

To be completed during the third year of the project

Ethics

Did your project undergo an Ethics Review (and/or Screening)?

Yes

If Yes, describe the progress of compliance with the relevant Ethics Review/Screening

All project partners and their reference national networks had already in place the IRB authorizations for the collection and the research use of primary human samples, covering the finalities that are in line with those of the approved project, and complying with local, national and EU regulations in matter of informed consent and other legal requirements.
As written in the original project after the funding acceptance, each partner has readily presented to the competent IRBs for formal registration of the funded project, allowing immediate access to the samples already available and covering for those that will be collected during the project.

Data Management Plan

Has a Data Management Plan been produced?

Yes

If yes, do you intend to publish this plan?

No

Problems

Have you had any relevant problems with the implementation of the work plan?

Yes

If Yes, please select the reason(s) that may explain the problems

[-] Difficulties in recruiting personnel
[-] Poor communication between project partners
[-] Change of one project partner
[-] One or more partners underperforming
[X] Experimental/technical difficulties
[X] Other

Please specify other reason

Delayed project activation for some partners

Meetings

Please list the project meetings face-to-face and/or virtual held in this reporting period

Record N° 1

Meeting type involving at least two partners of the project

(e.g. consortium meetings, WP meetings, workshops, or others)

Consortium meeting

Main purpose

Administrative updates on the:
- Activation of the grant from National funding agencies
- Generation of the Consortium agreement

Scientific tasks:
- Update on the optimization of the technologies and techniques for the descriptive and functional profiling of EM samples
- Status on the generation of a common spreadsheet
- Status on EM sample accrual

Partners involved

IRCCS Ospedale San Raffaele (P1)
UKSH Universitätsklinikum Schleswig-Holstein (P3)
IRCCS Istituto Europeo di Oncologia (IEO) (P4)
Medical University of Graz (P5)
Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6)

Young researchers

Please indicate the young researchers involved so far in the project, and for those interested in receiving information on networking activities from TRANSCAN-3, please add their e-mail

Record N° 1

Career level of young researchers *

Research assistant (without PhD)

Email

If they are interested in receiving information on networking activities from TRANSCAN-3

Name *

Kordevani Fatemeh

Record N° 2

Career level of young researchers *

PhD student

Email

If they are interested in receiving information on networking activities from TRANSCAN-3

Name *

Schmidt Dominik

Record N° 3

Career level of young researchers *

Post doc (1-2 years after PhD)

Email

If they are interested in receiving information on networking activities from TRANSCAN-3

Name *

Hossein Emami

Record N° 4

Career level of young researchers *

PhD student

Email

If they are interested in receiving information on networking activities from TRANSCAN-3

Name *

Mangione Marta

Record N° 5

Career level of young researchers *

PhD student

Email

If they are interested in receiving information on networking activities from TRANSCAN-3

Name *

Panagiota Chaida

Record N° 6

Career level of young researchers *

Research assistant (without PhD)

Email

If they are interested in receiving information on networking activities from TRANSCAN-3

Name *

Ofner Lara

Record N° 7

Career level of young researchers *

Early career researcher (2-7 years after PhD)

Email

If they are interested in receiving information on networking activities from TRANSCAN-3

Name *

Andersson Rebecca

Record N° 8

Career level of young researchers *

Research assistant (without PhD)

Email

If they are interested in receiving information on networking activities from TRANSCAN-3

Name *

Medici Catalina

Communication and Dissemination of results

Record N° 1

Type of activity*
Presentation at international scientific event

Type
Oral Presentation

Partners involved*
IRCCS Ospedale San Raffaele (P1)

Where*
Riga, Latvia

Date*
17/10/2023

Link*
file:///Users/toffalori.cristina/Downloads/transcan-3_abstracts_book_1st_symposium_riga_october_20 23.pdf

Description*
Overview of the PIXEL project

Notes
None

Scientific publications

Please note: only publications acknowledging TRANSCAN-3 funding shall be listed.

Record N° 1

Type of Publication
Peer-reviewed articles

Title of the journal or equivalent, number, date, relevant pages
Nature Cancer

Title of the scientific publication
Targeting TGF-β-activated kinase-1 activation in microglia reduces CAR T immune effector cell-associated neurotoxicity-syndrome

Publisher, Place of Publication
Provisionally accepted

DOI
Not yet available

Year
2024

Authors
please specify also the affiliation

Janaki Manoja Vinnakota1,2, Francesca Biavasco1, Marius Schwabenland3, Chintan Chhatbar3, Rachael C. Adams1,4,5, Daniel Erny3, Sandra Duquesne1, Nadia El Khawanky1,6,7, Dominik Schmidt1,2, Viktor Fetsch1,2, Alexander Zähringer1, Henrike Salié8, Dimitrios Athanassopoulos1, Lukas M. Braun1,2 Rebeka N. Javorniczky1, Jenny N.H.G. Ho1, Katrin Kierdorf3, Reinhard Marks1, Ralph Wäsch1, Federico Simonetta9, Geoffroy Andrieux10, Dietmar Pfeifer1, Gianni Monaco3,11,12, Christian Capitini13, Terry J Fry14, Thomas Blank3, Bruce R. Blazar15, Eva Wagner16, Matthias Theobald16, Clemens Sommer17, Matthias Stelljes18, Christian Reicherts18, Astrid Jeibmann19, Jens

Is/Will open access provided to this publication?
No

Journal Impact Factor
22,70

Schittenhelm20, Camelia-Maria Monoranu21, Andreas Rosenwald21, Martin Kortüm22, Leo Rasche22, Hermann Einsele22, Philipp T. Meyer23, Joachim Brumberg23, Simon Völkl24, Andreas Mackensen24, Roland Coras25, Michael von Bergwelt-Baildon26, Nathalie L. Albert27,28, Laura M. Bartos28, Matthias Brendel28,29,30, Adrien Holzgreve28, Matthias Mack31, Melanie Boerries10,32, Crystal L Mackall33, Justus Duyster1, Philipp Henneke34, Josef Priller35, Natalie Köhler1,36, Felix Strübing37, Bertram Bengsch8,32, Marco Ruella38, 39, Marion Subklewe26,27, Louisa von Baumgarten27,40, Saar Gill38,39, Marco Prinz3,41*, Robert Zeiser1,32,41*

* M.P. and R.Z.: These authors jointly supervised this work

1 Department of Medicine I - Medical centre - University of Freiburg, Faculty of Medicine,
University of Freiburg, Germany
2 Faculty of Biology, Albert-Ludwigs-University, Freiburg, Germany
3 Institute for Neuropathology, Medical Faculty, University of Freiburg, Germany
4 Faculty of Medicine, The University of Queensland, Brisbane, Australia
5 QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia.
6 Department of Medicine III, School of Medicine, Technical University of Munich, Munich, Germany
7 Center for Translational Cancer Research (TranslaTUM), School of Medicine, Technical University of Munich, Munich, Germany.
8 Department of Medicine II - Medical centre - University of Freiburg, Faculty of Medicine,
University of Freiburg, Germany
9 Division of Hematology, Geneva University Hospitals Geneva, Switzerland
10 Institute of Medical Bioinformatics and Systems Medicine, Medical Center - University of
Freiburg, Germany.
11 Single-Cell Omics Platform Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany
12Institute for Transfusion Medicine and Gene Therapy, Medical Center – University of Freiburg, Freiburg, Germany
13 Pediatric Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD.
14 Center for Cancer and Blood Disorders, Children's Hospital Colorado and Department of Pediatrics, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA.
15 Masonic Cancer Center and Department of Pediatrics, Division of Blood & Marrow
Transplant & Cellular Therapy, University of Minnesota, Minneapolis, Minnesota, USA
16 Department of Hematology and Medical Oncology, Johannes Gutenberg-University Medical Center, Mainz, Germany
17 Institute of Neuropathology, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany
18 Department of Medicine/Hematology and Oncology, University of Münster, Münster, Germany
19 Institute of Neuropathology, University Hospital Münster, Münster, Germany
20 Department of Neuropathology, Institute of Pathology and Neuropathology, University Hospital Tübingen, Tübingen, Germany
21 Institute of Pathology, University of Würzburg, Würzburg, Germany
22 Department of Internal Medicine 2, University Hospital of Würzburg, Würzburg, Germany
23 Department of Nuclear Medicine - Medical centre - University of Freiburg, Faculty of
Medicine, University of Freiburg, Germany

24 Department of Internal Medicine 5, Hematology and Oncology, University Hospital
Erlangen, Erlangen, Germany
25 Department of Neuropathology, University Hospital Erlangen, Erlangen, Germany
26 Department of Medicine III, Hematology/Oncology, University Hospital, Ludwig-Maximilians
Universität (LMU) Munich, Munich, Germany, Germany
27 German Cancer Consortium (DKTK), partner site Munich, German Cancer Research Center (DKFZ), Heidelberg, Germany
28 Department of Nuclear Medicine, University Hospital, LMU Munich, Munich, Germany
29 German Center for Neurodegenerative Diseases (DZNE), Munich, Germany
30 Munich Cluster for Systems Neurology (SyNergy), Munich, Germany
31 Department of Nephrology, University of Regensburg, Regensburg, Germany
32 German Cancer Consortium (DKTK), partner site Freiburg, German Cancer Research
Center (DKFZ), Heidelberg, Germany
33 Center for Cancer Cell Therapy, Stanford Cancer Institute, USA
34 Division of Pediatric Infectious Diseases, Medical Centre - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany
35 Department of Psychiatry Technischen Universität München (TUM), Munich, Germany
36 CIBSS – Centre for Integrative Biological Signalling Studies, University of Freiburg, Freiburg, Germany
37 Center for Neuropathology and Prion Research, University Hospital, LMU Munich, Munich,
Germany
38 Center for Cellular Immunotherapies, University of Pennsylvania, Philadelphia, PA, USA
39 Division of Hematology-Oncology, Department of Medicine, Hospital of the University of
Pennsylvania, Philadelphia, PA, USA
40 Division of Neuro-Oncology, Department of Neurosurgery, University Hospital, LMU
Munich, Munich, Germany
41 Signalling Research Centres BIOSS and CIBSS – Centre for Integrative Biological
Signalling Studies, University of Freiburg

Record N° 2

Type of Publication
Peer-reviewed articles

Title of the scientific publication
Oncogenic calreticulin induces TGF-β expression and Treg expansion in the bone marrow microenvironment as a mechanism of immune escape

DOI
Not yet available

Authors
please specify also the affiliation

Dominik Schmidt1,2, Cornelia Endres1,2, Rouven Höfflin3, Geoffroy Andrieux4, Melissa Zwick1,2, Nikolaos Karantzelis1, Felix Staehle1, Sandra Duquesne1, Miriam Mozaffari1, Dietmar Pfeifer1, Heiko Becker1, Heike Pahl1, Bruce R. Blazar5, Alexander Zähringer1, Justus Duyster1, Tilman

Title of the journal or equivalent, number, date, relevant pages
Cancer Research

Publisher, Place of Publication
In revision

Year
2024

Is/Will open access provided to this publication?
No

Journal Impact Factor
13,31

Brummer6,7, Melanie Boerries4,7, Marcelo Toledo8, Julian Baumeister8, Itay Tirosh3, Ann Mullally9, Natalie Köhler1,10, Steffen Koschmieder8 *, Robert Zeiser1, 7, 10 *

* R.Z. and S.K. are co-senior authors.

1 Department of Medicine I - Medical centre - University of Freiburg, Faculty of Medicine,
University of Freiburg, Germany
2 Faculty of Biology, Albert-Ludwigs-University, Freiburg, Germany
3 Weizman Institute, Rehovot, Israel
4 Institute of Medical Bioinformatics and Systems Medicine, Medical Center - University of
Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany
5 Masonic Cancer Center and Department of Pediatrics, Division of Blood and Marrow
Transplantation, University of Minnesota, Minneapolis, Minnesota, USA
6 IMMZ, University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
7 German Cancer Consortium (DKTK), Partner site Freiburg, a partnership between DKFZ and Medical Center - University of Freiburg
8 Department of Hematology, Oncology, Hemostaseology, and Stem Cell Transplantation, Faculty of Medicine, RWTH Aachen University, and Center for Integrated Oncology, Aachen Bonn Cologne Düsseldorf (CIO ABCD), Aachen, Germany
9 Division of Hematology, Dana Farber Cancer Institute, Boston, USA
10 Signalling Research Centres BIOSS and CIBSS – Centre for Integrative Biological Signalling Studies, University of Freiburg

Impact of the project results

Please tick and describe the major achievements of the consortium.

- [–] **Launching a new product**
- [–] **Launching a new service**
- [X] **Implementation of new methodologies/method/process**

  Optimization of the technologies and techniques for the descriptive and functional profiling for the analysis and comparison of EM and BM primary leukemia samples, as described in the “Scientific Section”
- [–] **Creation of a platform available to a community**
- [–] **Identification of new genes**
- [–] **Development of innovative screening systems**
- [–] **Identification and characterisation of biomarkers**
- [–] **Validation of biomarkers**
- [–] **Generation of novel model systems (animal or cellular)**
- [–] **Development of innovative therapies**
- [–] **New medical treatments**
- [–] **New medical devices/equipment**
- [–] **Prevention**
- [–] **LICENCES**
- [–] **CREATION OF A NEW ENTERPRISE**
- [–] **Other**

Capacity building - Mobility (if applicable)

Please, list below the mobility of human resources between partners occurred within the framework of this project (academic staff, PhD students, master students, undergraduate students, etc.)

Capacity building - Jobs (if applicable)

Please list below the number of jobs created within the framework of the current project (Post-Doc fellowships & Contracts)

Record N° 1

Partner * IRCCS Ospedale San Raffaele (P1) - Italy	**Name** * Kordevani Fatemeh
Type * Fellowship	**Gender** * F
New/ Continuation * New	**Duration of the fellowship/contract** (months/years) * 12 months

Record N° 2

Partner * IRCCS Ospedale San Raffaele (P1) - Italy	**Name** * Moronetti Lorenza
Type * Fellowship	**Gender** * F
New/ Continuation * New	**Duration of the fellowship/contract** (months/years) * 7 months

Record N° 3

Partner * IRCCS Ospedale San Raffaele (P1) - Italy	**Name** * Petrovich Giulia
Type * Fellowship	**Gender** * F
New/ Continuation *	**Duration of the fellowship/contract** (months/years)

New

*

12 months

Record N° 4

Partner *

Universitätsklinikum Freiburg (P2) - Germany

Name *

Schmidt Dominik

Type *

Contract

Gender *

M

New/ Continuation *

New

Duration of the fellowship/contract (months/years) *

12 months

Record N° 5

Partner *

UKSH Universitätsklinikum Schleswig-Holstein (P3) - Germany

Name *

Hossein Emami

Type *

Contract

Gender *

M

New/ Continuation *

New

Duration of the fellowship/contract (months/years) *

30 months

Record N° 6

Partner *

IRCCS Istituto Europeo di Oncologia (IEO) (P4) - Italy

Name *

Mangione Marta

Type *

Fellowship

Gender *

F

New/ Continuation *

New

Duration of the fellowship/contract (months/years) *

36 months

Record N° 7

Partner *

Name *

Medical University of Graz (P5) - Austria

Panagiota Chaida

Type *

Contract

Gender *

F

New/ Continuation *

New

Duration of the fellowship/contract (months/years) *

36 months

Record N° 8

Partner *

Medical University of Graz (P5) - Austria

Name *

Ofner Lara

Type *

Contract

Gender *

F

New/ Continuation *

New

Duration of the fellowship/contract (months/years) *

12 months

Record N° 9

Partner *

Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6) - Spain

Name *

Andersson Rebecca

Type *

Contract

Gender *

F

New/ Continuation *

New

Duration of the fellowship/contract (months/years) *

36 months

Record N° 10

Partner *

Fundació Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) (P6) - Spain

Name *

Medici Catalina

Type *

Contract

Gender *

F

New/ Continuation *

New

Duration of the fellowship/contract (months/years) *

24 months

Stakeholder engagement

Briefly describe the activities implemented to involve
a) patients 'organisations
b) civil society (open days, events)
c) policy makers
d) industry and innovators

Patents

Have any of your project results been patented or licensed either nationally, at EU level or internationally?

If you consider relevant, please provide additional details concerning the patents, licences and other outputs

If details need to be treated confidentially, please indicate as such.

Added value of cooperation in a consortium

Added value of the collaboration in the transnational project is *

As high as expected

In the field below please describe the expectancy fulfilment based on actual outcomes of the project

Free text (max. 250 words for annual reports; max 500 words for final report)

The strength of this project relies on the integrative system biology approaches proposed that will allow to profile and model the entirety of the complex system and intricated interplay between AML cells and microenvironment of EM localizations, and define the determinants that distinguish between EM and BM AML localisations.
The proposal places together an extraordinary team of researchers focused on the immunobiology of hematological malignancies and innovative technologies to study an under investigated type of myeloid malignancy. The combination of these expertise will not only provide a state-of-the-art description of single aspects of the target disease, but have the same cases characterized at the highest possible level for multiple aspects, including the ex vivo and in vivo functional behaviour. The optimization of these powerful technologies will be also of high relevance for future studies from the partners and from other investigators. Moreover, since EM AML represents a peculiar hybrid between hematological and solid tumors, this project will render possible a scientific advancement not only in the field of the immunobiology and immunotherapy of hematological malignancies, but also in the context of other cancers.

New collaborations

Have new collaborations been made with groups outside the consortium, since the project started, due to this project? *

No

Has the consortium or any consortium partners applied to other Calls due to this project? *

Yes

Please indicate How many proposals were submitted in Transnational calls*

0

Please indicate How many proposals were granted in Transnational calls*

0

Please indicate How many proposals were submitted in

National calls*

1

Please indicate How many proposals were granted in National calls*

1

Milano, 08/03/2024

Luca Vago