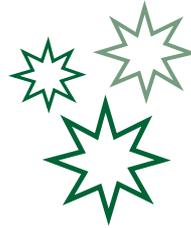


NEWSLETTER

CHRISTMAS 2020



SPECIAL EDITION

20th SWISS BRIDGE AWARD

Zurich, November, 2020



SWISS BRIDGE AWARD 2020

Two winners share the prize money of CHF 500'000

The prestigious European award for young scientists was announced this year for the 20th time since its inception. The SWISS BRIDGE Scientific Jury selected a promising topic fitting the occasion: Basic and translational research in childhood cancer. Some 50 applicants from 13 different countries took part in the competition, two of whom were finally selected by Prof. Dr. Gordon McVie, Chairman of the SWISS BRIDGE Scientific Jury, after a thorough evaluation by his great team.

This year's SWISS BRIDGE Award goes to a research group from Germany and a research group from Switzerland!

Ana S. Guerreiro Stücklin, MD PhD



Department of Oncology
and Children's Research Center,
University Children's
Hospital Zurich

Project title:

Targeting the kinome
in oncofusion-driven
pediatric gliomas

David T. W. Jones, PhD



Hopp Children's Cancer Center Heidelberg
(KITZ) & German Cancer Research Center
(DKFZ) Group Leader
"Pediatric Glioma Research Group"

Project title:

Identifying novel therapeutic targets for
childhood brain tumors using CRISPR
in vivo screens in orthotopic mouse models



This year's award ceremony, which was planned for October 21, unfortunately had to be cancelled due to the current restrictions. Once the situation permits it again, this wonderful evening event will be rescheduled in 2021.

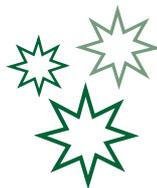


Ana S. Guerreiro Stücklin, MD PhD

Date of birth 22/07/1980

Department of Oncology
and Children's Research Center,
University Children's Hospital Zurich

Project title:
Targeting the kinome
in oncofusion-driven
pediatric gliomas



Summary:

Background: Brain tumors account for the majority of morbidity and mortality in pediatric cancer patients. While studying congenital brain tumors, we recently described a distinct group of pediatric gliomas harboring key targetable rearrangements in a cluster of highly homologous receptor tyrosine kinases (RTK).

The role of these ALK/ROS1/NTRK/MET oncofusions in gliomagenesis remains largely unknown but their detection has immediate clinical implications. While eagerly anticipating encouraging responses to targeted agents, concerns for development of drug resistance under selective therapeutic pressure are mounting.

Overall goal and specific aim:

The overall goal of this project is to deliver detailed molecular insights into a group of pediatric brain tumors to inform the next generation of clinical trials. We aim to: (1) investigate the mechanisms underlying glial transformation by RTK oncofusions; (2) understand the kinome-wide impact of targeted therapies; and (3) harness combination treatments to enhance antitumor activity and prevent drug resistance in RTK-rearranged gliomas.

Approach and Expected Results:

At a first level – oncofusion functional characterization – we develop and deploy models that mimic the human disease, to characterize cellular functions regulated by fusion proteins. At a second level – pathway elucidation – we use technological advances (kinase microarrays) to profile the kinome and elucidate the downstream pathway activity, both at baseline and upon treatment with current RTK inhibitors.

We further seek clinical translation and determine the expression of pathway components associated with drug resistance in patient tumor samples (nanoString 3D). Lastly, at a third level – therapy optimization – combining these results, we design and validate new combination strategies with enhanced anti-tumor activity and preventing drug resistance.

Significance:

This project clarifies the molecular basis of RTK oncofusion-driven pediatric gliomas and evaluates strategies to prophylactically prevent resistance in the setting of targeted treatments. Successful completion provides the preclinical bases for future clinical studies aimed at improving survival and increasing the quality of life for survivors.

WANT TO SUPPORT THIS PROJECT?
WE LOOK FORWARD TO HEARING FROM YOU.





David T. W. Jones, PhD

Date of birth 22/04/1983

Hopp Children's Cancer Center Heidelberg (KiTZ)
& German Cancer Research Center (DKFZ)
Group Leader "Pediatric Glioma Research Group"

Project title:
Identifying novel therapeutic targets
for childhood brain tumors using CRISPR
in vivo screens in orthotopic mouse models



Summary:

Pediatric high grade glioma (pHGG) is an aggressive tumor entity with poor prognosis that urgently requires novel treatment options. The proposed project aims to identify these by an unbiased search for tumor vulnerabilities followed by an in vivo validation and subsequent preclinical studies. To this end, multiple mouse models for pHGGs will be characterized regarding their utility for CRISPR screening approaches by using a non-targeting barcode library.

Suitable models will then be screened with model-specific, custom gRNA libraries to identify gRNA targets that lead to tumor regression upon knockout.

The use of complementary immunocompetent allograft- and human xenograft-models will provide an unparalleled amount of in vivo CRISPR screening data across a spectrum of molecularly- defined subtypes of this tumor entity.

A detailed bioinformatic analysis will unravel multiple insights into tumor biology and model-specific traits. Identified genes representing potential new therapy targets will undergo separate validation by inducing expression of the respective single-gene gRNA during tumor growth in vivo.

Residual tumors will be analyzed by single cell RNA sequencing to investigate tumor adaptation after gRNA expression (i.e. possible resistance mechanisms), and to logically plan combination therapies.

Ultimately, these combination treatments will be evaluated in a preclinical setting. A close, well-established collaboration with the Heidelberg University Hospital and pediatric early-phase clinical trial networks provides a clear path to allow the direct translation of promising findings into clinical application.

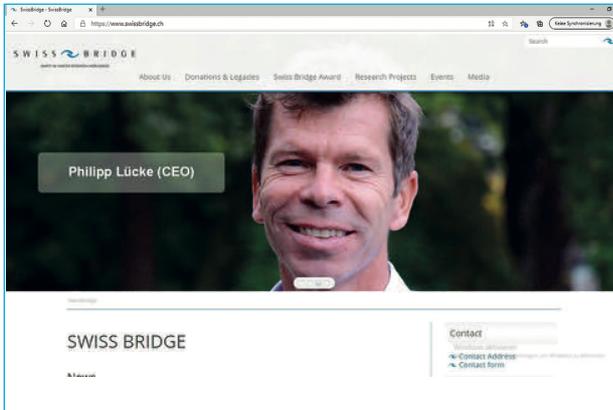


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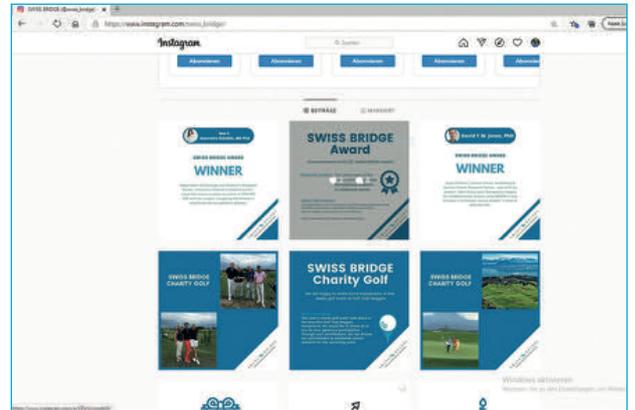


SWISS BRIDGE now on Social Media

and with a new website at www.swissbridge.ch



Homepage



Instagram

SWISS BRIDGE

Golf Charity Event 2020

Once again it was a wonderful day of golf at Golfclub Meggen near Lucerne and a lovely evening. Many thanks to all of the loyal participants and the generous sponsors who make this annual event possible.

We will offer this event again in 2021, and we're already looking forward to seeing you!



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