

One Medicine – One Oncology: Animal Cancer Registry

Symposium

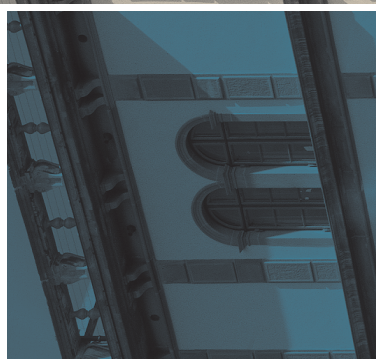
Thursday and Friday, June 9–10, 2016

Collegium Helveticum, Schmelzbergstrasse 25, 8006 Zurich

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Cancer registries are a key feature of any epidemiological study or prevention and control strategy. Specifically, canine and feline tumor registries are intended to assist in different aspects of research on tumor pathogenesis and epidemiology as well as treatment and prevention methods for both animals and humans. Traditionally, comparative cancer research is based on murine models using xenografts and transgenic models. Despite the undeniable importance of these models, they are limited in their representation of some essential features defining human cancer, including genomic instability, growth over longer time periods, function of the immune system, and a significant heterogeneity of tumor cells, microenvironment, and tumor stroma. To fill the gap between the research on tumors under experimental conditions and that on spontaneous tumors in pets reflecting most features of human cancer, canine and feline tumor registries are important for tumor epidemiology. Domestic animals like dogs and cats share the same living environment and are exposed to the same risk factors, therefore acting as sentinels for recognition of environmental factors implicated in oncogenesis. There are striking histopathological, anatomical, genetic, and biomolecular similarities between canine, feline and human tumors. Breed and sex-specific risks can be used to discover new disease triggers, and pathways can be tested and targeted for possible treatment. Somatic mutations and genome alterations in companion animals can help to evaluate human mutations.

Comparison of data from canine and feline tumor registries has recently gained increasing interest in the context of the “One Medicine – One Pathology” concept, part of the “One Health Initiative”. Our present research: “One Medicine – One Oncology – Incidence and Geographical Distribution of Tumors in Dogs and Cats in Switzerland 1955–2008”^{1–8}, is based on extensive data collection and interpretation with the aim of learning more about interdisciplinary human animal comparison as well as genetic and environmental aspects of spontaneous tumor development in dogs and cats. As a necessary initial step we wish to emphasize the importance of the registration of canine and feline tumors in Switzerland, as this may lead to a better understanding of animal and human tumor etiologies.

- ¹ Grüntzig, K., Graf, R., Hässig, M et. al. (2015). The Swiss Canine Cancer Registry: A retrospective study on the occurrence of tumors in dogs in Switzerland from 1955 to 2008. *Journal of Comparative Pathology*, 152, 161–171.
- ² Graf R, Grüntzig K, Hässig M et al. (2015) Swiss Feline Cancer Registry: a retrospective study of the occurrence of tumours in cats in Switzerland from 1965 to 2008. *Journal of Comparative Pathology*, 153(4):266–277.
- ³ Graf R, Grüntzig K, Boo G, et al. Swiss Feline Cancer Registry 1965–2008: the Influence of Sex, Breed and Age on Tumour Types and Tumour Locations. *J. Comp. Path.* 2016, <http://dx.doi.org/10.1016/j.jcpa.2016.01.008>.
- ⁴ Boo G, Fabrikant SI, Leyk S, 2015a. A novel approach to veterinary spatial epidemiology: dasymetric refinement of the Swiss Dog Tumor Registry data. *ISPRS Annals of Photogrammetry, Remote Sensing and Spatial Information Sciences II-3/W5*, 263–269.
- ⁵ Boo G, Fabrikant SI, Leyk S, Andreas Pospischil A, 2015b. An innovative geographical approach to spatial epidemiology dasymetric refinement of dog tumor incidence location data in Switzerland. *GE-OMED 2015*, Florence (Italy).
- ⁶ Pospischil A, Folkers G. How much reproducibility do we need in human and veterinary pathology? *Exp Toxicol Pathol.* 2015; 67:77–80. doi: 10.1016/j.etp.2014.11.005. Epub 2014 Dec 4. PMID: 25483119.
- ⁷ Pospischil A, Grüntzig K, Graf R, Boo G, Folkers G, Otto V, Fabrikant SI. One Medicine – One Oncology – Incidence and Geographical Distribution of Tumors in Dogs and Cats in Switzerland from 1955–2008. 3rd GRF One Health Summit 2015, 04–06 October 2015 • Davos • Switzerland, 108–111.
- ⁸ Grüntzig K et al. Swiss Canine Cancer Registry 1955–2008: Influence of sex, breed and body size on tumour development (submitted).

Program Schedule

Thursday, June 9, 2016

08:30	Welcome
08:45	Prof. Jakob Zinsstag One Health – the Added Value of Closer Cooperation of Human and Animal Health
09:45	Dr. Martin Adam, Dr. Ivan Curjuric Human Cancer Registration in Switzerland: Insights and Outlook
10:30	Coffee Break
11:00	Ramona Graf One Medicine – One Oncology: Incidence of Tumors in Dogs and Cats in Switzerland 1955–2008
11:45	Gianluca Boo Spatial Distribution of Dog Cancer in Switzerland: A Case Study of Skin Tumors During the Period 2008–2013
12:30	Lunch Break
14:15	Dr. Marta Vascellari Animal Tumour Registry of Venice and Vicenza Provinces (North-Eastern Italy) from 2005 to 2015: Incidence of Spontaneous Tumours in Dogs and Cats
15:00	Julia Wu Companion Animals in Comparative Oncology: one Medicine in Action
15:45	Short Break
16:00	Dr. P-J Noble Companion Animal Surveillance
16:45	Prof. John Reif Animal Sentinels of Cancer and Other Disorders: Closing the Loop between Animal and Human Health
17:45	End of Symposium

Program Schedule

Friday, June 10, 2016

8:30–12:30 In Depth Discussion with Presenters and Scientists
and Fellows at the Collegium Helveticum

Abstracts

Dr. Martin Adam and Dr. Ivan Curjurić
(Directors of the cancer registry Aargau)

Human Cancer Registration in Switzerland: Insights and Outlook

Human Cancer monitoring is the systematic collection of information on new cancer cases, the extent of the disease and therapies. The collected cancer data can be used to evaluate the efficacy of screening and other prevention programs, to look for trends over time and identify risk groups, to support cantonal health institutions in the quality management of diagnostic and therapeutic interventions and to serve as data basis for epidemiological and clinical cancer research.

In 2016, 14 cantonal cancer registries cover 23 cantons and 94% of the Swiss population. Human cancer registration in Switzerland is organized at the cantonal level by the local cantonal cancer registry. After data collection, classification and validation, the data is aggregated at national level by the National Institute for Cancer Epidemiology and Registration (NICER). Cancer registration coverage is since 2006 complete in the French- and Italian-speaking parts of Switzerland, while in the German-speaking part 3 cantons (Schaffhausen, Schwyz, Solothurn) do not have a cantonal cancer registry. The forthcoming law on Swiss cancer registration, which has recently been passed by the Swiss parliament, aims to establish an effective national cancer monitoring system by requiring all cantons to contribute data on cancer to a central Swiss registry. Having Swiss-wide data on human cancer incidence and prevalence at hand will ultimately allow precise estimates of cancer burden and treatment outcomes and deliver high-quality, representative data for national and international comparisons.

Comparative studies of Swiss-wide data collected in animal cancer registries and human cancer monitoring can yield important insights into cancer causation. Studying the similarities and differences between the cancer burden of animals and humans with respect to tumor type, temporal-spatial distribution and course of disease can produce information about common environmental and endogenous predictors, but also species-specific etiological mechanisms. Such transdisciplinary research by Swiss human and veterinarian cancer epidemiologists may very well contribute to synergistic benefits under the framework of the “One Health” concept and result in closer future collaboration to the benefit of better cancer control for both, humans and animals.

The presentation will highlight cornerstones and current challenges in human cancer registration in Switzerland and establish first comparative links to veterinary cancer registration and research.

Gianluca Boo, M.Sc.

(Affiliated Researcher at the Collegium Helveticum)

Spatial Distribution of Dog Cancer in Switzerland: A Case Study of Skin Tumors During the Period 2008–2013

Most of the existing research on companion-animal cancer disregards associations between the spatial distribution of outcomes and the presence of potential environmental risk factors. The result of such investigations might be of great significance and possibly signal the presence of exposures that also pose a potential risk to humans. However, the establishment of such linkages is currently challenged by well-known limitations in the spatio-temporal extent of companion-animal cancer registries.

The Swiss Canine Cancer Registry (SCCR) is an exceptional data source consisting of canine diagnostic records reported countrywide during the last 60 years. Diagnoses are classified according to human oncology standards (ICD-O-3) and spatially aggregated to compute cancer incidences at the municipality level. Furthermore, incidences can be adjusted for the underlying characteristic of the risk dog population, as dog registration has been mandatory in Switzerland since 2006.

I present the SCCR through a case study of the spatial distribution of skin tumors in Switzerland for the period 2008–2013. This is the most common tumor type among dogs as it is the easiest to detect. In particular, I provide characteristics and spatial distributions of the dog population and tumor incidences, further highlighting regions at high risk. In addition, I demonstrate the way in which spatial heterogeneity of tumor risk can be modeled through selected explanatory factors, part of which are also relevant to humans.

Ramona Graf, M.Sc.

(Scientific Researcher at the Collegium Helveticum)

One Medicine – One Oncology: Incidence of Tumors in Dogs and Cats in Switzerland 1955–2008

Cancer registries provide data for epidemiological studies that allow for incidence calculation, risk factor identification and development of prevention and control strategies, as well as treatment and spatial evaluation. The study of companion animal tumors offers benefits not only for animal epidemiology, but also for comparative epidemiological, pathogenic and therapeutic research.

As part of our research project “One Medicine – One Oncology – Incidence and Geographical Distribution of Tumors in Dogs and Cats in Switzerland 1955–2008”,

two animal cancer registries were prepared. Pathology records of 121'963 dogs and 51'322 cats, compiled between 1955 and 2008 by three veterinary diagnostic laboratories based in Switzerland, were classified according to the tumor type, malignancy, and physical location following the guidelines of the International Classification of Oncology for Humans (ICD-O-3). Firstly, epidemiological analyses on the occurrence of tumors in dogs and cats were carried out, examining sex, breed, neuter status and age differences.^{1,2} In an extended study, using a multiple logistic regression model, we analyzed the most common tumor types and tumor locations, their distribution and relative frequency over the period of the study^{3,4}. I present selected findings from the Swiss feline and the Swiss canine cancer registry.

¹ Grüntzig, K., Graf, R., Hässig, M et. al. (2015). The Swiss Canine Cancer Registry: A retrospective study on the occurrence of tumors in dogs in Switzerland from 1955 to 2008. *Journal of Comparative Pathology*, 152, 161–171.

² Graf R, Grüntzig K, Hässig M et al. (2015) Swiss Feline Cancer Registry: a retrospective study of the occurrence of tumours in cats in Switzerland from 1965 to 2008. *Journal of Comparative Pathology*, 153(4):266–277.

³ Graf R, Grüntzig K, Boo G, et al. Swiss Feline Cancer Registry 1965–2008: the Influence of Sex, Breed and Age on Tumour Types and Tumour Locations. *J. Comp. Path.* 2016, <http://dx.doi.org/10.1016/j.jcpa.2016.01.008>

⁴ Grüntzig K et al. Swiss Canine Cancer Registry 1955–2008: Influence of sex, breed and body size on tumour development (submitted).

Dr. P-J Noble

(Lecturer Small Animal Teaching Hospital, School of Veterinary Science, University of Liverpool, UK)

Companion Animal Surveillance

Disease surveillance is a vital part of protecting species and allowing targeted action to emerging threats. Most surveillance activities are mandated by government, driven by global trade agreements. The end result are the OIE-listed (previously reportable) diseases, which the UK government is now required to survey for. The processes established to monitor for listed diseases have also allowed surveillance of non-listed diseases, ultimately leading to the creation of a mature (and still evolving), largely government-funded, surveillance programme coordinated in the UK by The animal and plant health agency (APHA), Scotland's Rural College (SRUC) and the Agri-Food and Biosciences Institute of Northern Ireland (AFBNI).

What about companion animals? Well, because small companion animals were not a prominent feature of world trade, they have historically been left behind. Clearly, some of the OIE-listed diseases can occasionally infect our small companion animals (e.g. Rabies, HPAl, Bovine tuberculosis, Aujeszky's disease virus), and so

companion animals are a part of surveillance for these diseases especially in the face of an outbreak. However, of 118 infections listed by the OIE, only two primarily affect companion animals. The lack of a requirement to survey and, in parallel, the lack of a legislated framework for companion animal surveillance, has arguably, over decades, created a void in our understanding of a wide range of important diseases in these populations, and with it, an relative inability to control them.

The paucity of small animal disease surveillance mandated a solution. This has been provided, thanks to a new area of science called “health informatics”, where electronic health data is reused for research and surveillance, we are now starting to see some of these information gaps being filled. SAVSNET (the Small Animal Veterinary Surveillance Network – www.SAVSNET.co.uk), a partnership between BSAVA and University of Liverpool, collects real-time electronic health data from ~10% of UK practices and laboratories, and reuses it for research and surveillance, recently becoming the provider of quarterly surveillance reports in the Veterinary Record. Along with other projects such as VetCompass (RVC), CEVM (University of Nottingham) and the Bristol cohort studies, we are now capturing “Big Data” on what happens in veterinary practice, and gaining new insight into all areas of companion health. Recent examples from SAVSNET include population demographics, use of antibiotics, tick activity and frequency of diarrhoea.

This is the beginning of a brave new era where Big Data sourced in practice is providing new opportunities to understand and respond to the diseases in our pets, as well as other species, notably humans. These data are also now being made available in real-time to provide local clinical knowledge to SAVSNET data providers. This feedback loop of data from practice being used in real-time for surveillance, and simultaneously, benchmarking our data providers, is an efficient model for future sustainability, and one which provides many opportunities to improve the health of the animals we work with and their owners.

This presentation will review the SAVSNET experience of developing small animal disease surveillance and discuss key technologies that are being used to implement this program in the UK.

Prof. John S. Reif, D.V.M., M.Sc. (med)

(Professor Emeritus Department of Environmental and Radiological Health Sciences Colorado State University Fort Collins, CO, USA)

Animal Sentinels of Cancer and Other Disorders: Closing the Loop between Animal and Human Health

The interactions between veterinary and human medicine were originally described in the 19th century as “One Medicine” by the German pathologist Rudolph Virchow and Sir William Osler, a physician who studied under Virchow. Like the “Canary in the Coal Mine”, using pet animals to identify environmental hazards for humans is an idea which had its origins in the 1960's with studies on air pollution, asbestos, pesticides and other exposures which might increase cancer risk among pets and their human companions. The concept has been recently re-popularized under the descriptor of “One Health”. However, for the most part, recent efforts have fallen short of developing a truly translational relationship between species with the exception of the obvious interactions in zoonotic diseases.

In the first part of this presentation, several seminal studies of cancer in pet animals will be reviewed briefly to provide a context for the remainder of the symposium. Secondly, our current work on exposure to mercury in a dolphin population in coastal Florida will be described. Identification of high concentrations of mercury in the tissues of wild dolphins led to testing the hypothesis that local human populations which share a common environment with the marine mammal may be at similar risk of exposure and the important attendant health effects known to result from that exposure. The study to be described clearly exemplifies the importance of an animal sentinel in identifying a public health hazard and is virtually unique in “closing the loop” between animal and human health.

Dr. Marta Vascellari, Katia Capello

(Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro, Italy)

Animal Tumour Registry of Venice and Vicenza Provinces (North-Eastern Italy) from 2005 to 2015: Incidence of Spontaneous Tumours in Dogs and Cats

Cancer registration represents a key tool for cancer surveillance, in both human and veterinary medicine. In April 2005, the Istituto Zooprofilattico Sperimentale delle Venezie implemented the Tumor Registry of dogs and cats living in Venice and Vicenza provinces, supported by a grant from the Italian Ministry of Health. A network of collaboration with the veterinary clinics was established, an accurate estimate of the canine and feline population living in Veneto region was performed, and the estimation of spontaneous neoplasms incidence in dogs and cats living in the catchment areas has been provided.

The canine and feline population of the Veneto Region, was estimated to be 849,229 (95% CI: 814,747 to 889,394), and 663,443 (IC95%: 626,585–737,159), respectively.

During the past 10 years (2005–2015), the Animal tumor Registry of the Venice and Vicenza provinces allowed the registration of 11,145 tumors in dogs, and 1,894 cases in cats. Overall, the incidence rate (IR) of spontaneous tumors in the dog population resulted to be 391 cases per 100,000 dogs/year, equally distributed between malignancies (IR 208) and benign tumors (IR 183). Pure-bred showed higher IRs than cross-bred (purebred IR 453 vs. cross-bred: 314); the females have an IR equal to 501 while the IR in males is 283. This difference is due to the high incidence of mammary tumors in female dogs. The most frequent cancers in dogs were mammary cancers (IR 52), testicular tumors (IR 45), soft tissue sarcoma (IR 24), mast cell tumors (IR 40) and lymphoma (IR 10). The IRs observed in cats was 82 cases per 100,000 of cats/year, with a rate of malignancies (IR 66) four times higher than that of benign tumors (IR 16). The females have a higher incidence rate than males (females IR = 85; male IR = 75), while purebred have a risk of developing cancer 1.4 times higher than crossbred. In cat population, the most represented tumors are soft tissue sarcomas (IR 23), mammary tumors (IR 16) and lymphomas (IR 8). This project has allowed to estimate the burden of cancer in the population at risk, considering individual and environmental risk factors and monitoring rates of cancer over time.

Julia Y. Wu, BSc, MPhil, MSc
(Immune Regulation Laboratory, The Royal Veterinary College,
University of London, UK)

Companion Animals in Comparative Oncology: one Medicine in Action

Cancer is a major cause of morbidity and mortality in companion animals. Epidemiological studies in dogs, for which most data are available, suggest that cancer kills 40 to 50% of individuals over the age of 10 years. Cancer in dogs resembles cancer in humans in various ways, including its long latency, clinical presentation and metastatic potential; its pathobiological characteristics, including tumour cell heterogeneity and suppressive microenvironment; its genomic instability and pharmacogenomic signatures, including chemoresistance; and its multifactorial nature, including both genetic and environmental risk factors. Increasing recognition of the inability of murine models to recapitulate all of these characteristics of human tumours and the frequent failure of such models to inform Phase II and III clinical trials has brought to light the huge potential value of spontaneous canine and, to a lesser extent, feline cancer in the drug discovery and validation pipeline, for the mutual benefit of all parties. The term ‘Comparative Oncology’ – the study of naturally occurring cancers in animals as models for human disease – has been

borne. Of the companion animals, the dog is the species in which the discipline of comparative oncology has shown most growth. A number of canine clinical studies informing human clinical trials have advanced oncology in many unanticipated ways. However, pharmaceutical companies generally remain hesitant to commit resources to canine clinical trials. While there are still many hurdles to overcome before clinical studies in pet animals, particularly dogs, become a routine part of drug development by Big Pharma, much has been achieved in the past decade and the tide is turning, slowly but surely. The next decade is poised to deliver a number of breakthroughs in cancer therapy, predicated on the exciting groundwork undertaken in the past five years or so.

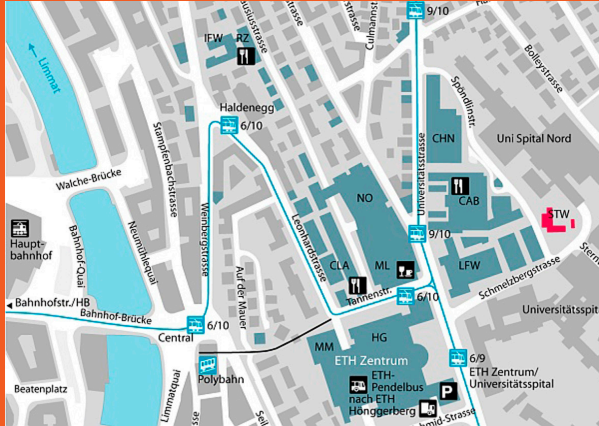
Prof. Jakob Zinsstag
(Swiss Tropical and Public Health Institute, Basel)

One Health – the Added Value of Closer Cooperation of Human and Animal Health

The inextricable linkage of human and animal health has been increasingly recognized in the past decades. However, human and veterinary medicine are often working so much in separation that human and animal health is affected. We define One Health (OH) as the added value in terms of human and animal health benefits, financial and other resource savings and improved environmental services compared to the two medicines working in separation. An integrated assessment of human and animal health requires methods capable of assessing effects on the animal – human interface. For example livestock mass vaccination against brucellosis is not profitable for the public health sector alone but becomes largely profitable from a societal perspective including all involved sectors. Other examples are provided from health services, rabies control, integrated antimicrobial resistance surveillance and joint laboratory infrastructure. Besides the large use of animals for the study of pathogenesis and therapy of tumors, implications of OH are for example integrated approaches to the surveillance of cancer in dogs and humans. Can dogs be sentinels for environmental exposure of humans? Large scale spatio-temporal dog-human studies could reveal such potential patterns. Conceptually OH is embedded in broader ecosystem approaches to health which can also be called health in social-ecological systems or health in human-environment systems which have particularly important implications for cancer research. In this way human and animal health improvements will be developed while considering social dynamics and sustained ecosystem services.

Venue

Collegium Helveticum, Semper-Sternwarte, Schmelzbergstr. 25, 8006 Zurich



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Contact

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Registration

Since the number of participants is limited, registration is necessary and will be processed in the order of arrival. Please register at reservation@collegium.ethz.ch (keyword: animal cancer registry). Deadline is June 3rd, 2016.

COLLEGIUM HELVETICUM
LABORATORIUM FÜR TRANSDISZIPLINARITÄT

IN GEMEINSAMER TRÄGERSCHAFT
VON UNIVERSITÄT ZÜRICH UND ETH ZÜRICH

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