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Translation Oncology Through the One Health Perspective

Translacijska onkologija skozi perspektivo enega zdravja

Key words

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Translational research, including translation oncology, bridges the gap between basic research and clinical practise by bringing together disciplines, resources, expertise and techniques to improve the prevention, diagnosis and treatment of various diseases. Veterinary medicine plays a critical and integral part in helping translate recent advancements in therapeutic opportunities from bench to bedside, helping animal and human patients alike. To connect and involve researchers from all areas of life sciences, it is also important to present the results to promote translational studies and share their importance (1).

Comparative oncology is part of the core concept of One Health which places veterinary medicine alongside human medicine and emphasizes the interconnectedness of animal and human health (2 – 3). This integrated approach is crucial not only in the field of infectious diseases, particularly zoonoses, including the treatment and rational use of antimicrobial and antiparasitic drugs, but also in addressing several non-communicable diseases, such as cardiovascular diseases and cancer, which represent major health challenges in both developed and developing countries. Several animal and human tumours are similar in their epidemiology, characteristics and clinical manifestations. Companion animals share their living environment with humans and are exposed to the same environmental risk factors for cancer. Furthermore, while we gain valuable insights from the similarities across species, we also learn from the differences in cancer susceptibility and pathogenesis (4). For example, translating knowledge of tumour suppressor mechanisms

Translacijske raziskave, vključno s translacijsko onkologijo, zapolnjujejo vrzel med temeljnimi raziskavami in klinično prakso s povezovanjem disciplin, virov, strokovnega znanja in tehnik za izboljšanje preprečevanja, diagnosticiranja in zdravljenja bolezni. Veterinarska medicina ima ključno vlogo pri prenosu novih načinov zdravljenja iz predkliničnih raziskav v klinično prakso, kar prinaša dobrobit tako bolnim živalim, kot ljudem. Pomembno je tudi seznanjanje širše javnosti z rezultati raziskav in njihovega pomena, z namenom spodbujanja translacijskih študij (1).

Primerjalna onkologija je sestavni del koncepta »eno zdravje,« ki veterinarsko medicino postavlja ob bok humani in poudarja medsebojno povezanost zdravja živali in ljudi (2–3). Ta integrirani pristop je ključen ne le pri nalezljivih boleznih, zlasti zoonozah in racionalni uporabi protimikrobnih ter antiparazitskih zdravil, temveč tudi pri obravnavi nenalezljivih bolezni, kot so bolezni srca in ožilja ter rak, ki predstavljajo velik zdravstveni izziv v razvitem in nerazvitem svetu. Veliko živalskih in človeških tumorjev ima podobno epidemiologijo, značilnosti in klinične manifestacije. Družne živali, ki si z ljudmi delijo življenjsko okolje, so posledično izpostavljeni istim okolijskim dejavnikom tveganja za nastanek raka. Poleg podobnosti med vrstami lahko pridobimo dragocena spoznanja tudi iz razlik v dovzetnosti za raka in patogenezi (4). Na primer, prenos znanja o mehanizmih tumorske supresije, pri živalih, na zdravje ljudi je omogočil nove poglede na strategije preprečevanja in zdravljenja

observed throughout the animal kingdom to human health provided novel perspectives on cancer prevention and treatment strategies, underscoring the importance of veterinary medicine and comparative studies in understanding the mechanisms of cancer development (5-9).

The large number of dogs represents a significant group of potential 'candidates' for studying various aspects of tumors, particularly since experts estimate that about half of all dogs are affected by some form of neoplastic disease. Given the absence of 'gold standards' for treatment in veterinary medicine, testing new approaches in dogs offers a faster and more humane way to evaluate novel treatments (10). Dogs have a shorter life expectancy than humans, so all processes are faster. Unlike preclinical studies where tumours are experimentally induced in selected animal models with specific characteristics, such as immunodeficiency, dogs spontaneously develop cancer, which may lead to more comparable disease progression or treatment response as in humans. Additionally, due to their shorter lifespan, dogs allow for the observation of long-term treatment outcomes and are ideal for pre-clinical trials which ultimately can benefit both, humans and dogs. In recent decades, animals, or 'animal patients,' have been recognized as valuable models for translating research to human medicine. The number of clinical trials, particularly involving dogs, is growing exponentially.

In several breed-specific cancers, the same genetic mutations are found as in humans. One such example is colorectal cancer (11). The information on canine cancer genetics and molecular signatures are still lagging behind the human medicine what hinders advancement of comparative cancer research and veterinary oncology. The Integrated Cancer Database (ICDC) (12) was established to further research on human cancers by enabling comparative analysis with canine cancer. It offers insights into the known biological characteristics and similarities between various types of cancer in humans and dogs. The database also includes information on experimental strategies and ongoing basic and clinical studies. In veterinary medicine, the main aim of the standards and guidelines for conducting clinical trials on animals is to ensure the animal's welfare or the best possible quality of life (13). Work with animals is regulated by national legislations and international standards, which are strictly aimed at ensuring good clinical and laboratory practise and, above all, ethical considerations. Clinical trials in dogs are therefore conducted at various stages of drug and treatment development to investigate safety, efficacy, pharmacological properties, biomarker discovery, interactions in combination therapies and minimal residual disease, which should be beneficial for both humans and animals (8, 10). This requires collaboration between human and animal researchers and clinicians.

An example of a successful collaboration and therapeutic strategy implementation is the development of electrochemotherapy and gene electrotransfer with plasmid DNA

raka, kar poudarja pomen veterinarske medicine in primerjalnih raziskav pri razumevanju mehanizmov razvoja raka (5-9).

Velika populacija psov, med katerimi jih vsaj približno polovica zboli za rakom, predstavlja pomembno skupino živali za preučevanje različnih vidikov raka. Zaradi odsotnosti »zlatih standardov« zdravljenja v veterinarski medicini je preizkušanje novih pristopov na psih hitrejše in bolj humano. Psi imajo krajšo življenjsko dobo, kar omogoča hitrejše prepoznavanje uspešnosti zdravljenja. Za razliko od predkliničnih raziskav, pri katerih proučujemo večinoma inducirane tumorje na laboratorijskih živalih z okrnjenim imunskim sistemom, se pri psih rak razvije spontano, kar vodi do bolj primerljivih podatkov o napredovanju bolezni in odzivu na zdravljenje kot pri ljudeh.

Pri nekaterih pasmah psov so bile ugotovljene enake genetske mutacije kot pri ljudeh, na primer raku debelega črevesa in danke (11). Podatki o genskih in molekularnih značilnostih pasjih rakov zaostajajo za humano medicino, kar ovira napredek primerjalne onkologije. Ustanovitev integrirane baze podatkov o raku (ICDC) (12) omogoča primerjalne analize med človeškimi in pasjimi tumorji. Podatkovna baza vključuje tudi informacije o eksperimentalnih strategijah ter bazičnih in kliničnih raziskavah. Glavni cilj smernic za klinične študije na živalih je zagotoviti dobrobit živali in najboljšo možno kakovost življenja (13). Klinične raziskave na psih potekajo v različnih fazah razvoja zdravil, z namenom proučevanja varnosti, učinkovitosti, farmakoloških lastnosti, odkrivanja biomarkerjev, kombiniranega zdravljenja in rezidualne bolezni, kar prinaša korist tako ljudem kot živalim (8, 10).Primer uspešnega sodelovanja med veterinarsko in humano medicino je razvoj elektrokemoterapije (EKT) in genskega elektroprenosa (GET) s plazmidno DNA za IL-12, kar sta ključni področji raziskav na Veterinarski fakulteti, Univerze v Ljubljani. EKT je naša raziskovalna skupina v veterinarsko prakso uvedla pred več kot 25 leti (14, 15). Do danes smo uspešno zdravili več kot 400 živali, vključno s psmi, mačkami (16), konji (17) in eksotičnimi hišnimi ljubljenčki (18, 19). Leta 2016 smo objavili standardni operativni postopek za EKT pri psih in mačkah (20). Ugotovili smo, da je EKT varna in učinkovita alternativa za lokalno zdravljenje različnih vrst tumorjev, hkrati pa ne povzroča funkcionalni motenj in ohranja odličen kozmetični izgled. Številne klinične študije so potrdile varnost in učinkovitost kombiniranega zdravljenja ter pozitiven vpliv na lokalni nadzor tumorja in napredovanje bolezni ter spodbujanja imunskega odziva v boju proti raku (21–27). V zadnji klinični raziskavi smo pokazali, da kombinacija EKT z GET IL-12 pri mastocitomih podaljša čas brez bolezni in brez napredovanja v primerjavi s samo EKT (26–27). Spodbudni rezultati v veterinarski onkologiji so omogočili izvedbo faze I intratumoralnega GET z IL-12 pri bolnikih z bazalnoceličnim karcinomom, objavljene leta 2025 (28). Ti rezultati kažejo, da sodelovanje med raziskovalci in zdravniki na področju humane in veterinarske medicine vodi k razvoju novih terapevtskih možnosti, ki koristijo

for IL-12, key areas of focus for our research group at the University of Ljubljana. Electrochemotherapy (ECT) was introduced in veterinary medicine by our group more than 25 years ago (14, 15).

Since then, we have successfully treated more than 400 animals: dogs, cats (16), horses (17) and exotic pets (18, 19). In 2016, we established and published a Standard Operating Procedure protocol of the ECT treatment in dog and cats (20). We found that ECT is a safe and effective alternative local treatment option for different tumour types in all treated animal species. Beyond providing a long-lasting objective response, including complete or partial response, it also offers excellent cosmetic outcomes, which are often more acceptable to owners than extensive surgery. Furthermore, in dogs, gene electrotransfer treatment (GET) with plasmid-encoded IL-12 was added to increase the local response and stimulate the patient's immune system response against cancer. Numerous clinical studies over the years have confirmed the safety of this novel treatment and positive effects on local tumour control and disease progression (21-27). We found that GET offers patients a good quality of life, as the side effects are minimal. This was the primary reason why owners considered this treatment method suitable and would choose it again if necessary (13). Additionally, in the last clinical study we showed that the combinational treatment of ECT with GET of IL-12 of mast cell tumours, resulted in prolonged disease free and progression free interval in comparison to ECT alone (26-27). Moreover, the encouraging results from veterinary oncology, using gene electrotransfer with IL-12 have facilitated the completion of phase I trial of phIL12 plasmid intratumoral gene electrotransfer in patients with basal cell carcinoma in head and neck region, published in 2025 (28).

Together, these results highlight how successful collaboration between researchers and clinicians in both animal and human medicine leads to the development of novel therapeutic opportunities benefiting both human and animal patients. Additionally, publications emphasizing comparative oncology, such as this special issue of Slovenian Veterinary Medicine, are crucial for sharing findings with the broader community and fostering further collaborations between human and animal medicine.

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tako ljudem kot živalim. Publikacije, kot je tudi ta posebna izdaja Slovenskega veterinarskega zbornika, so ključne za širjenje ugotovitev in spodbujanje nadaljnjega sodelovanja med obema področjema.

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