RFA Concept:
Canine Cancer Immunotherapy Network (K9CIN)

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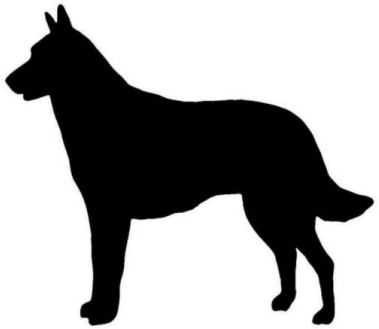
Why might *pet* dogs be a good patient model for translation?

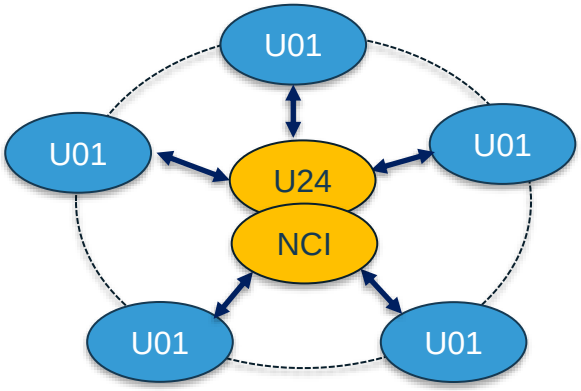
- Spontaneous, naturally occurring tumors at high frequencies
- Tumor heterogeneity, course of disease and treatment responses similar to humans
- Immunocompetent host
- Shorter lifespan and compressed disease progression timeline compared to humans
- Ability to test investigational drugs in early or minimal disease states (often no standard of care and different regulatory requirements)
- High degree of cooperation from pet owners



https://actavetscand.biomedcentral.com/articles/10.1186/s13028-018-0414-4

Cancer Moonshot-funded Canine Immunotherapy Network
(Progress at end of year 3 of 5 years funding)

PRE-medical Cancer Immunotherapy Network for PRECINCT Canine Trials



Best combination of TME modulators (high dose losartan + sunitinib); results led to opening of a phase 1 clinical trial in pediatric osteosarcoma

Combination of new CD200 checkpoint target peptide+ tumor lysate vaccine; data contributed to the FDA approval of the IND to support a phase 1 clinical trial in adult glioblastoma

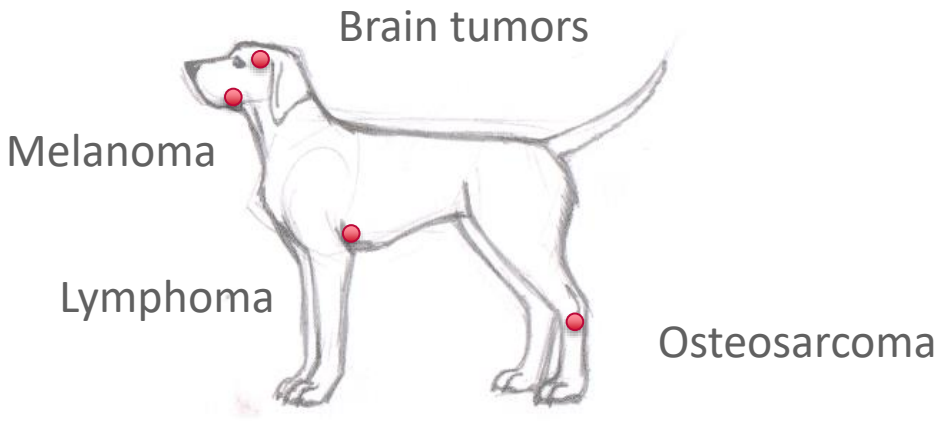
Support of development and release of Nanostring canine IO panel (>800 genes)

- Harmonized immune monitoring
- Addresses limitations of canine flow cytometry reagents

TME = tumor microenvironment

Areas not covered by PRECINCT

- Not all cancer types (e.g., bladder, mammary, thyroid cancers)
- Missing combinations with other therapies (especially radiation therapy)
- Limited cell therapies for cancer (e.g., CAR T, NK cell therapies)
- No anti-PD-1/L1 or anti-CTLA-4 immune checkpoint antibody therapies (will likely be available by the time the RFA is funded)



(covered in PRECINCT)

Purpose of the new RFAs

We request **set-aside funding and review** for a Canine Cancer Immunotherapy Network to support companion canine clinical trials in naturally occurring tumors using immunotherapeutic agents alone or in combination with other modalities with the **end goal** of informing cancer therapeutics in humans.

This will provide an opportunity for NCI to take a leadership role and build on its initial investments.

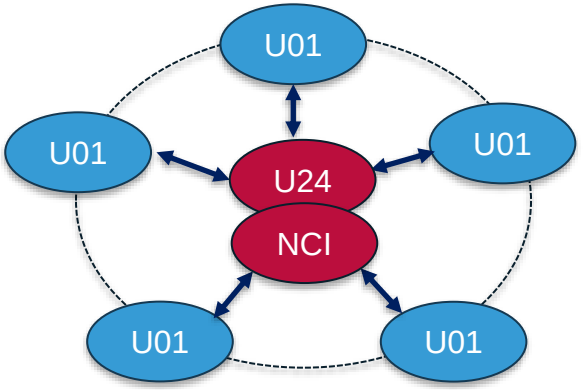
Current NCI Portfolio Analysis in Canine Immunotherapy

Mechanism	#mouse	#canine	Description (canine)
R01	208	2	STING immunotherapy; cancer vaccines
U01	26	7*	5 PRECINCT, 1 IOTN, 1 IRCN
U24	1	1*	PRECINCT coordinating center
U54	3	1*	IOTN, includes universal CAR T cell testing in canines
other	200	2	1 R37 (calreticulin nanoparticles), 1 P01 (radiation therapy and immunotherapy)
total	438	13	

R-type grants (non-Cancer Moonshot)
Canine - 3
Mouse - >200

Cancer Moonshot Canine Immunotherapy Network RFAs (2017):
27 U01 applications received, 5 funded
5 U24 applications received, 1 funded

Implementation plan for the RFA



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U01

Requirements

- provide published or preliminary data to support a canine clinical trial and correlative studies
- proposed trial must include therapeutic modulation of the TME or must elicit direct immune-mediated destruction of cancer (e.g., via adoptive immune cell therapy)
- immunophenotyping of tumor, peripheral blood, and other relevant tissues

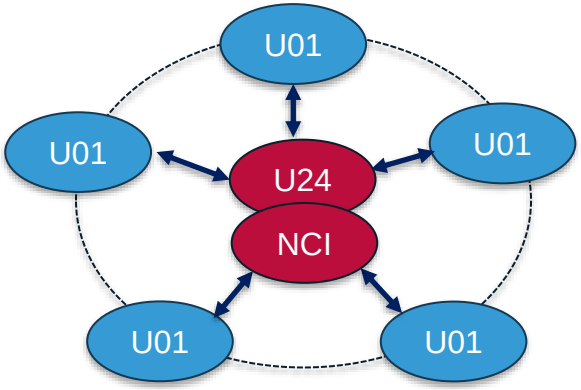
Priorities

- combinations of immunotherapy/TME-modulating therapy with radiation therapy or other therapies (targeted therapies, chemotherapies or other immunotherapies)
- protocols varying content, timing and sequence of combination therapies to best inform translation to human clinical trials
- longitudinal collection of tumor biopsies
- tumor DNA sequencing, transcriptomics and other “omics”

Examples

- a focused canine immunotherapy clinical trial or a series of pilot clinical trials followed by a larger focused clinical trial
- CAR T cell therapy with or without additional therapies

Implementation plan for the RFA



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U24

- Coordinate monthly virtual and annual in person steering committee meetings (steering committee will have U24, U01, NCI extramural and intramural staff, and expert advisors)

- Harmonize and submit canine clinical data to the already existing ICDC via a data coordinating center, develop SOPs for submission for the veterinary community at large

- Assign earmarked supplemental funding to U01 centers with projects proposing intra-network collaborations or projects nearing translation to humans ($100K DC set aside per year for years 2-5, carryover will be permitted). NCI program staff will have final approval of U24 prioritization and funding of discretionary projects.

ICDC = Integrated Canine Data Commons

Budget

- Total costs per year per award: $0.57 M
- RFA set-aside for year 1: ~$3.42 M (includes 5 U01s and 1 U24 at $570K each, translates to about $375K DC per year)
- Total 5 year cost: $17.1 M
- To be awarded in FY2022

Justification for use of the RFA mechanism

- Insufficient representation in the NCI portfolio (3 R01-type grants funded)

Justification for review in an NCI special emphasis panel

- No CSR review specialized for veterinary cancer research
- Single receipt date for U24 and U01s to allow for coincident funding of the network

Justification for use of the Cooperative Agreement mechanism

- Substantial programmatic involvement - Allows intramural and extramural staff to facilitate not only the conduct of the canine clinical trials, but to facilitate data sharing with the community through the ICDC
- U24 can coordinate data harmonization among the U01 sites
- After consultation with NCI, U24 can accelerate progress of one or more groups per year with earmarked funding from the U24 budget
- Second stage, focused U01 combination clinical trials can benefit from information gained from U01 pilot trials
- Ability to facilitate use of NCI resources

Successful outcomes at end of 5 years

- For immunotherapy combinations, successful translation to a phase I human clinical trial or readiness for translation to a phase I human clinical trial

- For cell therapy grants (e.g., CAR T), treatment of a canine cancer with adoptively transferred immune cells, establishment of baseline therapeutic conditions relevant to humans to which combinations and varied sequencing of combinations can be added

- Submission of harmonized, multi-site clinical and correlative data to the ICDC

- Advances that continue NCI/DCTD investment in building this underdeveloped model

Team

Connie Sommers – IOB/DTP/DCTD
Anju Singh – IOB/DTP/DCTD
Marc Ernstoff – IOB/DTP/DCTD

Toby Hecht – TRP/DCTD

Amy LeBlanc – COP/CCR

Mike Espey – RRP/DCTD

Suzanne Forry – PTGB/DTP/DCTD

Lori Henderson – CTEP/DCTD
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