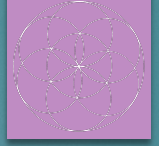


Precision Oncology and Integrative Medicine – contradiction or synergy?

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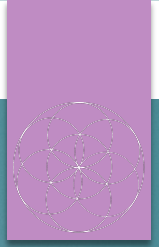
DIRECTOR OF SYNTHESIS CLINIC, CO-CHAIR BRITISH SOCIETY FOR INTEGRATIVE ONCOLOGY, FELLOW OF THE COLLEGE OF MEDICINE



Introduction – Dr Nina Fuller-Shavel

- ▶ Degrees in Natural Sciences and Medicine from the University of Cambridge
 - ▶ Background in cellular and molecular biology, distinction in Pathology, winner of the Henry Roy Dean Prize
- ▶ Postgraduate degrees in nutrition and integrative medicine and additional qualifications in herbal medicine, yoga and mindfulness
- ▶ Fellow of the College of Medicine
- ▶ Co-Chair of the British Society for Integrative Oncology
- ▶ Director of Synthesis Clinic (UK) – an award-winning multidisciplinary integrative medicine practice specialising in women’s health and integrative cancer support for solid tumours with a specialist interest in breast and gynaecological cancers (in collaboration with oncology teams)
- ▶ Research interests in precision cancer medicine (MSc University of Oxford) and integrative cancer support
 - ▶ Member of the conference committee for ECIM 2021 and reviewer for integrative oncology abstracts
- ▶ Educator – training for medical and nutrition professionals in integrative medicine for women’s health and integrative oncology (systems approach to cancer)

Session outline



- ▶ Review what integrative medicine and integrative oncology is
- ▶ Why does it matter?
- ▶ Thinking about the intersection with precision oncology – contradiction or synergy?

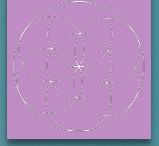
Integrative oncology

Integrative oncology definitions

- ▶ Integration of **evidence-informed conventional, psychological, nutritional, lifestyle and complementary medicine** in cancer care to support better quality of life, improve resilience, minimise the side effects of treatment and improve outcomes (BSIO definition)
- ▶ “Integrative oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment.” (Claudia Witt and SIO team)

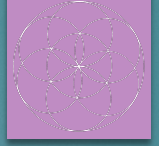


Why bother?



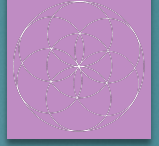
- ▶ Your patients are already doing it!
 - ▶ Based on various sources and variation based on location, between 40% and 90% of cancer patients use complementary medicine
 - ▶ Average likely around 50%
 - ▶ Australian range - 17% to 87% of cancer patients
 - ▶ Demographics - younger, female, having higher education, earning a higher income and having previously used CAM
 - ▶ Saying 'no' to everything means hidden risk and internal conflict for the patient, it does not mean compliance
 - ▶ Safe integrative oncology – being open and honest (mutual), ensuring appropriately qualified and experienced practitioners are on the case, ideally regular interprofessional communication

What does integrative oncology have to offer?



- ▶ A sense of agency and empowerment for your patients
 - ▶ Supporting resilience vs learned helplessness
- ▶ Expanded toolkit to support:
 - ▶ Cancer prevention
 - ▶ Pre-habilitation for better treatment tolerance and recovery
 - ▶ Managing side effects of treatment and opportunities for improving outcomes
 - ▶ Faster recovery following active treatment and better management of recurrence risk
 - ▶ Care of patients with metastatic disease – both in living well with cancer and at the end of life

Integrative oncology



- ▶ Is/should be:
 - ▶ a **rational and personalised** integration of the best in conventional, psychological, lifestyle and complementary medicine
 - ▶ whole-person oriented and addresses physical, emotional, mental and spiritual needs
 - ▶ supportive of targeted, personalised medication use where necessary without over-medicalising
 - ▶ about caring for people, not mindless protocols
 - ▶ evidence-based medicine - combining the best available research evidence, clinical expertise and patient values

Integrative oncology consultation

Lifestyle management

- Nutrition and diet
- Physical activity and exercise
- Sleep hygiene
- Stress management

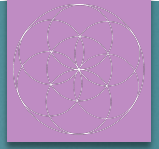
Herb and supplement consultation

- Assess and address CAM expectations
- Evaluate safety and potential herb-drug interactions
- Discuss evidence and advise on appropriate herb or supplement use in the cancer setting

Integrative medicine for symptom control

Symptom	Pain	Fatigue	Insomnia	Anxiety
Modality	<ul style="list-style-type: none"> • Acupuncture³⁰ • Massage³³⁻³⁵ • Meditation⁶¹⁻⁶⁴ 	<ul style="list-style-type: none"> • Exercise¹⁴⁻¹⁶ • Yoga^{7,47} • Acupuncture^{30,32} 	<ul style="list-style-type: none"> • CBT-I^{22,23} • Yoga^{7,47} • Tai chi^{7,25} 	<ul style="list-style-type: none"> • Meditation¹⁰ • Yoga¹⁰ • Massage^{34,35}
Symptom	Nausea and vomiting	Neuropathy	Dry mouth	Hot flashes
Modality	<ul style="list-style-type: none"> • Acupuncture¹⁰ • Acupressure¹⁰ 	<ul style="list-style-type: none"> • Acupuncture³⁰ • Massage⁶⁵ 	<ul style="list-style-type: none"> • Acupuncture³⁰ 	<ul style="list-style-type: none"> • Acupuncture³⁰ • Hypnosis⁶⁶ • Yoga^{67,68}

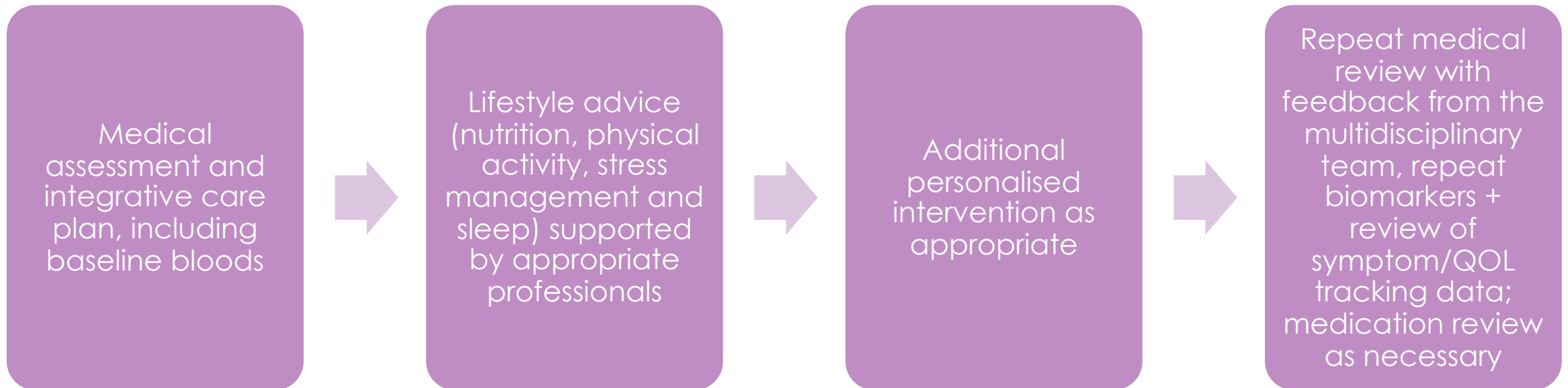
Example of
integrative
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framework



Our clinic team and referrals

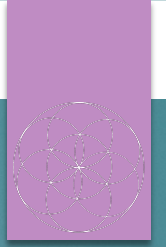
- ▶ Lead medical doctor with supporting team
 - ▶ Individualised assessment including clinical history +/- examination, oncology imaging, test results and review of plan; additional testing as appropriate (liquid biopsies, specialised blood tests)
 - ▶ Personalised plan based on therapeutic aims/stages and patient needs and goals – medication review; lifestyle as core (nutrition, physical activity, sleep and stress management/psychoemotional wellbeing); additional targeted support (checked for interactions) +/- referral for other therapies
 - ▶ Regular monitoring – symptom/QOL scores, blood tests
- ▶ Nutrition team
- ▶ Cancer exercise specialist referrals
- ▶ Physiotherapy, rehabilitation Pilates and ScarWork in-house
- ▶ Emotional wellbeing coaching
 - ▶ Referrals for psychology +/- trauma therapy as appropriate
- ▶ Referrals for specific therapies, e.g. acupuncture during chemotherapy re: N&V and CIPN etc

Care pathway



Integrative Oncology and Precision Oncology

How can this help within precision oncology?



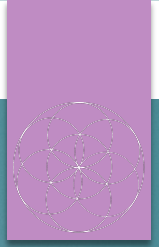
- ▶ Managing side effects from targeted therapies
- ▶ Improving outcomes, managing MDR and potential treatment synergy
 - ▶ Immunotherapy and the gut microbiome – minimising antibiotic use, supporting *Bifidobacteria* and *Akkermansia* levels (FMT being extensively studied but accessibility is an issue, dietary/nutraceutical modulation is far more widely applicable)
 - ▶ Specific targets that do not yet have a pharmaceutical allocation (potential benefit, requires more research but review risk-benefit)

Managing side effects – example

- ▶ Lapatinib and fasting - compared to bedtime administration, lapatinib administration after overnight fasting may reduce its toxicity without diminishing its therapeutic efficacy.
 - ▶ 140 breast cancer patients enrolled in the JBCRG-16/Neo-LaTH randomized phase 2 trial
 - ▶ A reduced risk of diarrhoea {adjusted hazard ratio (HR), 0.51, 95% confidence interval (CI), 0.27-0.89, $p = 0.018$ }, and rash {adjusted HR, 0.37; 95% CI, 0.17-0.70, $p = 0.002$ } was seen in BB (before breakfast) versus AB (at bedtime)
 - ▶ ?treatment synergy – animal studies show that fasting increases the ability of common TKIs, including erlotinib, gefitinib, lapatinib, crizotinib and regorafenib, to block cancer cell growth, to inhibit MAPK signalling pathway and to strengthen E2F-dependent transcription inhibition

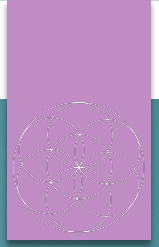
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Managing side effects – PI3K inhibitors and metabolic compromise



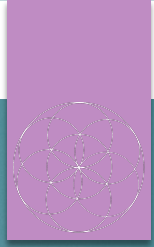
- ▶ Hyperglycemia is a common, on-target adverse effect that impairs treatment efficacy and increases the rate of treatment delays, dose reductions, and discontinuation
- ▶ When metformin is not effective, VLCD and SGLT2i may be effective – early data

Example of treatment synergy (chemotherapy)



- ▶ Curcumin and FOLFOX for CRC
 - ▶ Phase IIa open label RCT – 28 metastatic CRC patients randomised to FOLFOX compared with FOLFOX + 2 g oral curcumin/d (CUFOX) - HR for PFS was 0.57 (95% CI: 0.24, 1.36; P = 0.2) (median of 171 and 291 d for FOLFOX and CUFOX, respectively) and for OS was 0.34 (95% CI: 0.14, 0.82; P = 0.02) (median of 200 and 502 d for FOLFOX and CUFOX, respectively). There was no significant difference between arms for quality of life (P = 0.248) or neurotoxicity (P = 0.223).

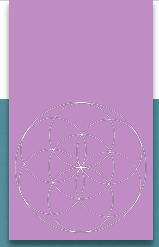
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Integrative oncology and MDR

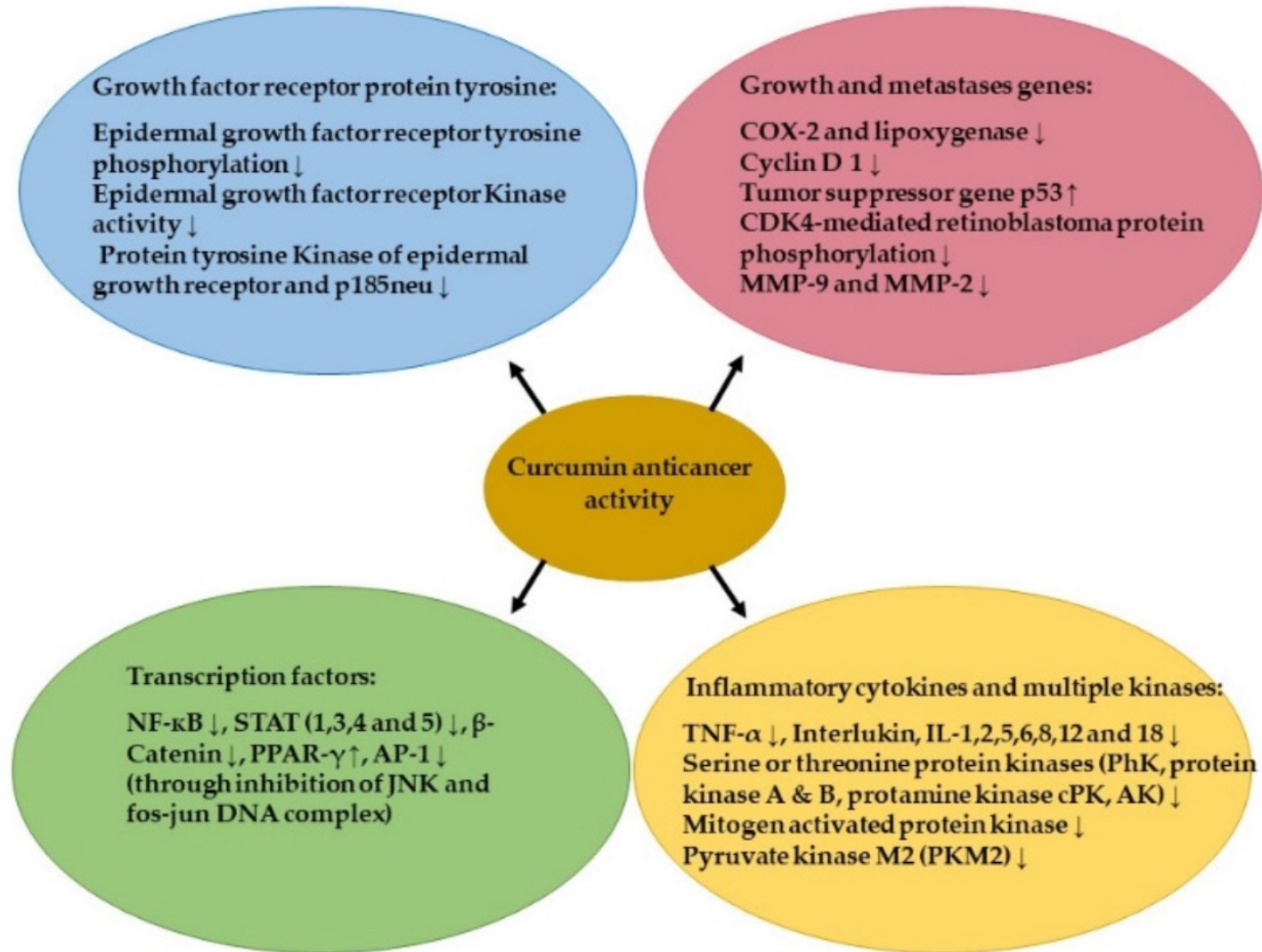
- ▶ Curcumin as modulator of P-gp by inhibiting both P-gp function and expression but issues with bioavailability and stability (products have been created with better profiles)
 - ▶ Nanoparticle approaches being studied, e.g. curcumin and paclitaxel
- ▶ Other natural compounds being studied, e.g. resveratrol, quercetin

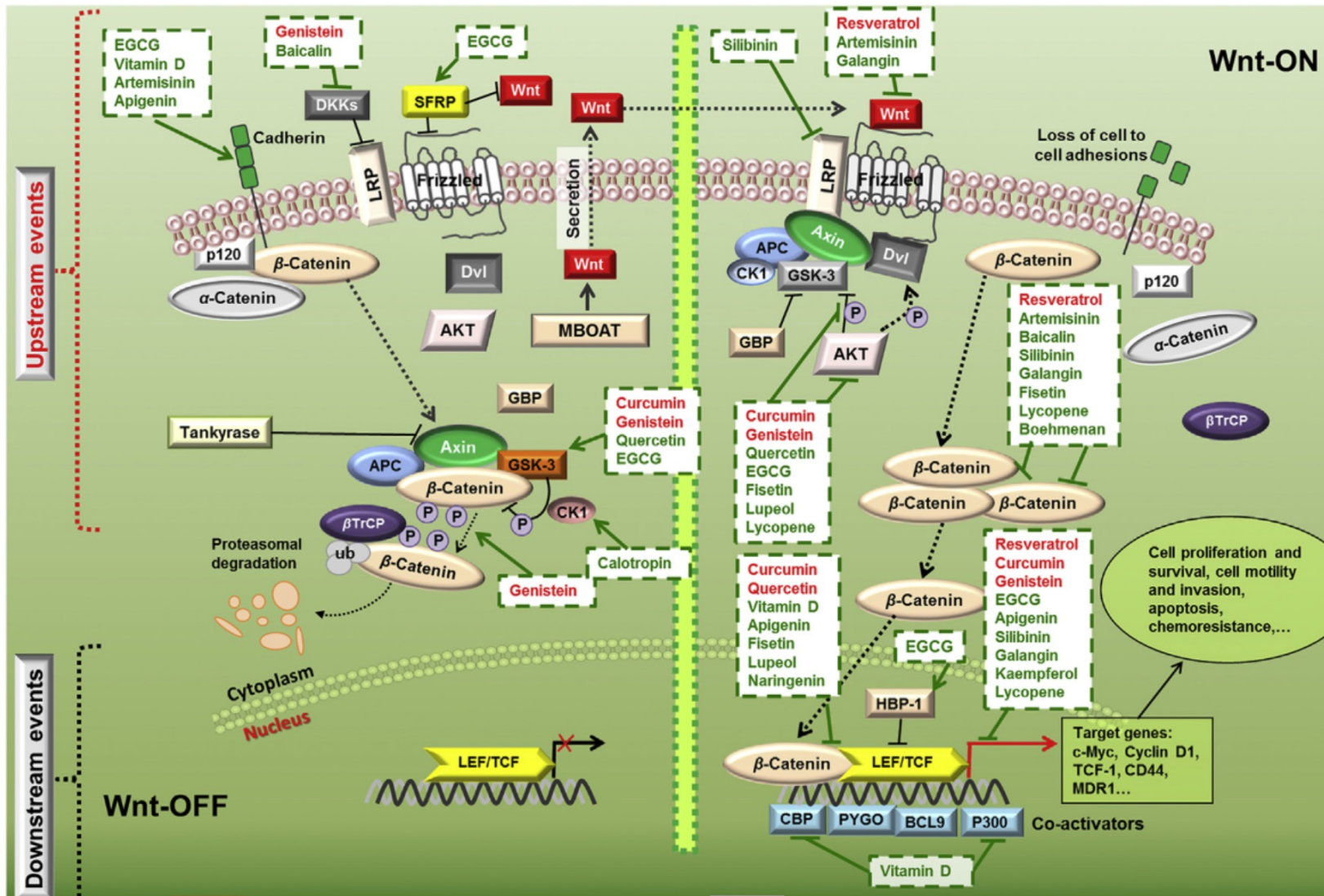
Potential for precise targeting – some early ideas and examples for further research



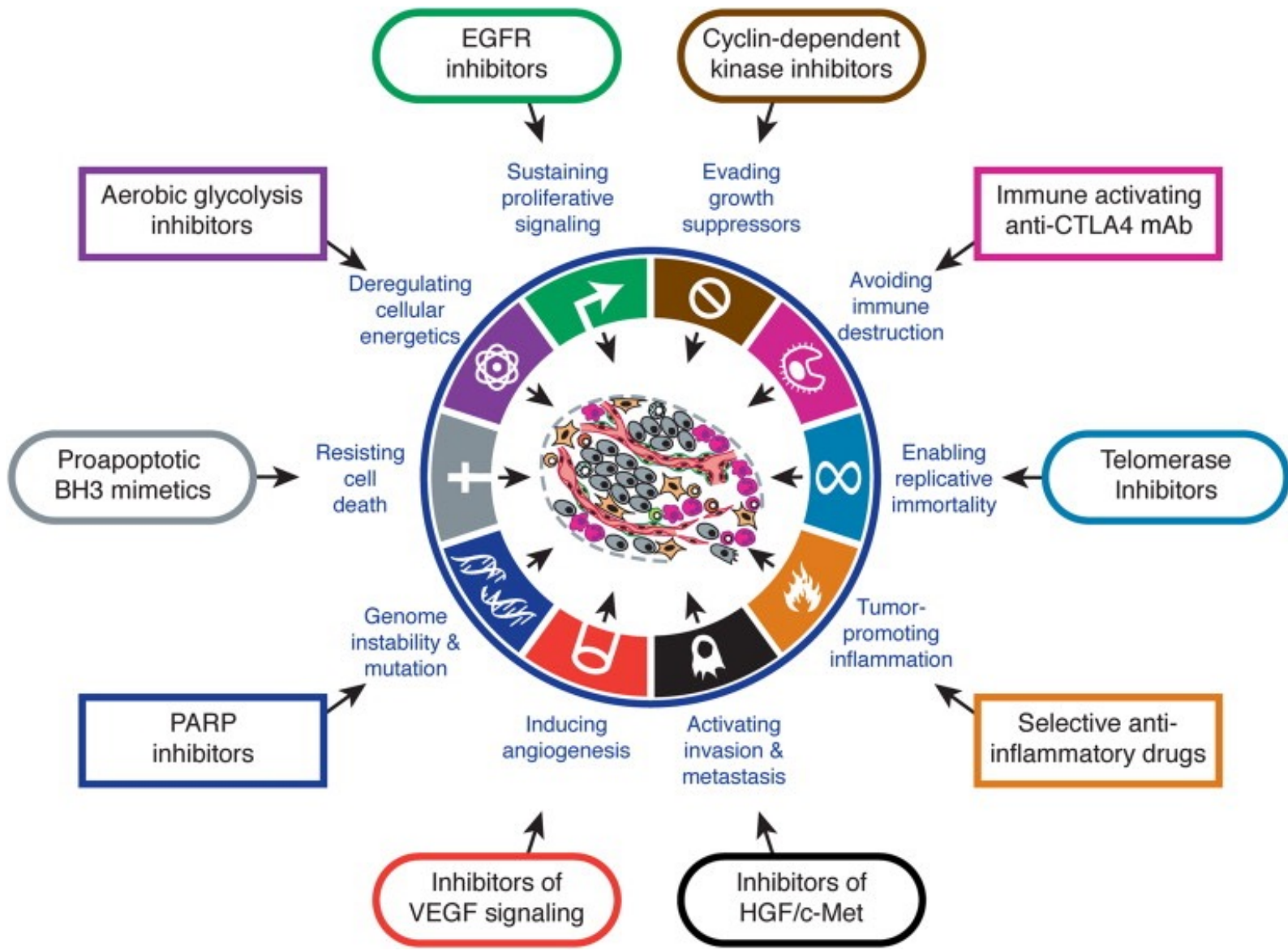
- ▶ TYMS upregulation
 - ▶ High dose melatonin (20-60mg) may be useful – early cell evidence, clinical evidence accumulating
- ▶ Quercetin/curcumin and Wnt/beta-catenin
- ▶ Multitarget effects of certain key substances
 - ▶ Curcumin may exert therapeutic effects via regulating miRNA expression (e.g., miR-1, miR-7, miR-9, miR-34a, miR-181, miR-21, and miR-19) which could lead to the regulation of underlying cellular and molecular pathways involved in cancer pathogenesis.
 - ▶ Quercetin could modulate multiple cancer-relevant miRNAs including let-7, miR-21, miR-146a and miR-155; quercetin modulates PI3K/Akt/mTOR, Wnt/beta-catenin, and MAPK/ERK1/2 pathway
 - ▶ And many more (**curcumin, resveratrol, berberine and quercetin** being some of the most common studied)
- ▶ Synergistic effects are possible, e.g. ginkgetin and resveratrol in suppressing VEGF-induced angiogenesis (animal work)

Curcumin





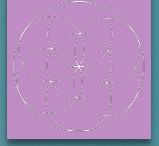
Wnt targeting pathway overview



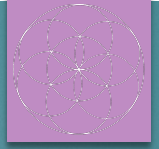
Hitting the hallmarks

Integrative oncology for maximizing effects and minimizing toxicity

Summary

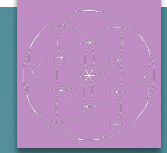


- ▶ Integrative oncology is a rational and personalised approach based on the synthesis of evidence-informed conventional, psychological, nutritional, lifestyle and complementary medicine in cancer care to support better quality of life, improve resilience, minimise the side effects of treatment and improve outcomes
- ▶ Appropriate use of evidence-informed lifestyle and complementary interventions can be of significant benefit in relieving side effects and improving tolerance of treatment, ideally as a part of integrative care plans.
 - ▶ True integration and alignment in purpose and the components of the management plan is essential
- ▶ More evidence is needed to assess the optimal timing and combination of interventions (including interaction with targets identified with precision oncology approaches and management of MDR) and to monitor impact on biomarkers and clinical outcomes
 - ▶ Multidisciplinary research teams with oncology, integrative medicine/nutrition/phytochemistry experts and laboratory scientists - rational project selection, interaction checking and appropriate outcome measures and biomarkers



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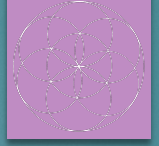
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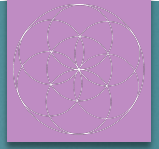
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