NEW ZEALAND SOCIETY OF ENDOCRINOLOGY

Agenda

Date: Friday, 10 Aug 2018
Time: 12 pm
Venue: Teleconferencing

Present: Greg, Stephen, Stella, Kathy, Ryan, Mike

Apologies: Richard, Susannah, Joe, Chris

Approve Minutes of previous meeting: Yes

Matters arising from Minutes dated 18 June 2018:
Actions required

- Greg to send email to NZSE members in regard to nomination for new management committee. DONE *(will send a follow-up email)*
- Greg to suggest amendments to NZSE constitution, particularly in regards to date of transfer to incoming management committee (change to February). DONE. *With minor suggestions, the Management Committee were happy for these suggestions to be circulated to the membership (for approval at the AGM).*
- Greg to nominate Prof. David Grattan for 2020 ICE Programme Organising Committee. DONE
- Greg to draft out regulations for a new postdoc/emerging researcher award based on the Endocrinology Society of Australia Servier Young Investigator Award. NOT DONE – *Action for next meeting.*
- Mike to find out the estimated budget for the 2018 Clinical Meeting. DONE

Incoming Correspondence:

25 July 2018 – *Michael Lewis, Diabetes Product Manager, Sanofi*
On behalf of Dr Shouten, requested for support from NZSE for sponsoring the upcoming Clinical meeting in November. Form was completed and returned on 27 July 2018.

Outgoing Correspondence:

02 July 2018 Greg emailed to NZSE member to Call for expressions of interest for the next New Zealand Society of Endocrinology Management Committee

01 Aug 2018 – Joe informed the approved new members to sign-up and pay using the new NZSE website

20 Aug 2018 – Joe informed Dr Eulalia Coutinho that her application for NZSE International Travel Award to assist her travel to the Androgen Excess – Polycystic Ovary Syndrome (AE-PCOS) meeting in Stockholm, Sweden has been successful. An NZ$800 was granted.

01 Aug 2018 – Greg emailed NZSE members informing the passing of Professor H Kaye Ibbertson, a founding and life member of the NZSE, on 12 July 2018

Items:

1. NZSE AGM 12:30pm, Tuesday 28 August, Rydges Hotel Queenstown (during the MedSci conference). President's and treasurers reports will be emailed to members will be emailed this week.
2. Clinical meeting update – the budget for this was missed from the agenda in error. It is appended to these minutes (Appendix 1). The budget anticipates that with 30 registrants, $6K of sponsorship would be required to break even.
3. Guidelines for Gender Affirming Healthcare for Gender Diverse and Transgender Children, Young People and Adults in Aotearoa, New Zealand - this document has received nationwide feedback and has already been endorsed by several groups working in this field nationally including the NZ Sexual Health Society, and Gender Minorities Aotearoa.
   NZSE agreed to add its endorsement to the guidelines.
4. Student travel award applications for MedSci meeting at Queenstown – none have been received yet, perhaps because all 4 student speaker entries are from Otago.
   It was noted that the abstracts for these student speaker entries should be circulated. They are appended to the minutes (Appendix 2).

Treasurer's Report:

Account balances:

Paypal account: $529.32
Business account: $2,210.17
Serious Saver account: $8,039.79
Term Deposit 1: $40,000.00 (Matures on 21st Dec)
Term deposit 2: $22,467.92 (Matures on 2nd Apr)
Term Deposit 3: $16,801.72 (Matures on 9th Jul)

Transactions since last meeting:

20 Jun 2018	$103.00	Greg Anderson	Reimbursement for Greymouse telecom.
27 June 2018	$800.00	Eulalia Coutinho	Travel Award
5 July 2018	$550.00	Dinamics	Speaker fees MedSci
9 Aug 2018	$718.76	Prefer	Website development

Bank accounts

A savings account has been opened to balance the maintaining the funding required for clinical meetings and transfers into term deposits. The savings account earns interest 2.2% interest and requires $20.00 to be transferred into it per month. A monthly automatic payment from the Business Account has been set up. If funds need to be transferred from the Serious Saver, the interest for the month is forfeited.

It is proposed that funds are transferred from the Business account if the amount is greater than $3000.00. It is proposed that funds should be transferred from the savings account into a term deposit if the quantity is greater than $10,000.00. Keeping this quantity in the savings account will facilitate the planning of clinical meetings if sponsors are slow to transfer funds to the society. The timing of transfers from the savings account into the term deposit should take the timing of upcoming clinical meetings into account. The ideal time for transfer of funds into term deposit is immediately after a profitable clinical meeting.

New Member applications: 10. All the members below were accepted - Joe Yip to send welcome letter. Action.

1. **India Sawyer*** indeeleigh@gmail.com **Student 3 Year Membership**
   Jul 6, 2018 University of Otago
2. **Teodora Georgescu** teodora.georgescu@otago.ac.nz **Post Doc Membership**
   Jul 9, 2018 University of Otago
3. **Bradley Jamieson*** jambr243@student.otago.ac.nz **Student Membership**
   Jul 11, 2018 University of Otago
4. **Manish Khanolkar** manishk@adhb.govt.nz **Full Membership**
   Jul 26, 2018 Greenlane Clinical Centre and Auckland University
5. **Eleni Hackwell*** eleni@ruarus.co.nz **Student Membership**
   Jul 31, 2018 University of Otago
6. **Rachel Nunn*** nunra751@student.otago.ac.nz **Student Membership**
   Jul 31, 2018 University of Otago
7. **Erik Wibowo** erik.wibowo@otago.ac.nz **Full Membership**
   Aug 1, 2018 University of Otago
8. **Brian Corley** geminus1@gmail.com **Full Membership**
   Aug 2, 2018 University of Otago, Wellington
9. **Kate Lee** kathryn.lee@auckland.ac.nz **Post Doc Membership**
   Aug 2, 2018 University of Auckland, Faculty of Medical and Healeth Sciences
10. **Shalini Kumar** kumsh868@student.oatgo.ac.nz **Student Membership**
    Aug 2, 2018 University of Otago

* MedSci student speaker prize contestants. See abstracts in Appendix 2.

Full members: 48
Postdoc members: 2
Student members: 7
Life Members: 10

Other Business: As part of a discussion regarding how we might spur interest in nominations for the next president, treasurer and secretary, it was suggested that we consisder establishing a paid secretary to carry some of the load of each. Action: Greg, Joe and Mike to list key tasks and estimate the hours/month that would be required (to bring to next meeting).

Meeting closed: 1 pm.

Next Meeting: 12 October.

Appendix 1: Draft Clinical Meeting Budget

Draft budget for the 2018 Clinical Conference

Clinical Endocrinology 2016						2018 Budget			2018 Budget			2018 Budget		
Total Costs (Incl. GST @ 15%)						delegates =	20		delegates =	30		Delegates =	40	
Description	Variable	Fixed	Total Budget			Variable	Fixed	Total Budget	Variable	Fixed	Total Budget	Variable	Fixed	Total Budget
Speakers costs	3,120	17,500	20,620		DIY (delegates)	0	0	0	0	0	0	0	0	0
			-											
Trainee day				Paid by Novartis	Not doing this	0	0	0	0	0	0	0	0	0
Welcome function	2,091	1,500	3,591		(teas and coffee)	0	0	0	0	0	0	0	0	0
					Novotel									
Conference Daily Package	3,038	1,000	4,038		(approx 85pp)	1700	600	2300	2550	600	3150	3400	600	4000
			-		Novotel									
Conference audio and visuals	-	2,500	2,500			0	500	500	0	500	500		500	500
					TBA ? Tram									
Conference Dinner	4,838	1,940	6,778	pp 165	$200	4000	0	4000	6000	0	6000	8000	0	8000
			-		DIY (Kahu)									
Conference packs	221	750	971		$40	$800	$0	800	$1,200	$0	1200	$1,600	$0	1600
					DIY (Kahu)									
Dinamics	1,972	6,325	8,297			0	1000	1000	0	1000	1000	0	1000	1000
Contingency						0	1000	1000	0	1000	1000	0	1000	1000
Additions	-	2,500	2,500		Person on the day		800	800		800	800		800	800
					16 hours *50									
Total	**15,279**	**34,015**	**49,294**			6500	3900	**10400**	9750	3900	**13650**	13000	3900	**16900**
Trainee day	3,304	1,624	4,928	Covered by Novartis										
Registrations					Registrations	(assuming 10k sponsorship)								
					(assuming 60% SMOs, 20% nurses, 20% trainees)									
SMOs	**29**	**$600**	**$17,400**			12	350	4200	18	350	6300	24	350	8400
Nurses	**9**	**350**	**3150**			4	0	0	6	0	0	8	0	0
Trainees						4	200	800	6	200	1200	8	200	1600
			20,550		Sponsorship			10000			10000			10000
								4600			**3850**			**3100**
					Registrations	(assuming 5k sponsorship)								
					(assuming 60% SMOs, 20% nurses, 20% trainees)									
						12	350	4200	18	350	6300	24	350	8400
						4	0	0	6	0	0	8	0	0
						4	200	800	6	200	1200	8	200	1600
					Sponsorship			5000			5000			5000
								-400			**-1150**			**-1900**

Appendix 2: Abstracts of MedSci student speaker contestants

Central prolactin action is required for maintaining lactational diestrus in mice

Hackwell, E.C.R[1], Ladyman S.R.[1], Brown, R.S.E.[1], Grattan, D.R.[1,2]

[1] Centre for Neuroendocrinology and Department of Anatomy, School of Biomedical Sciences, University of Otago, Dunedin, NZ. [2] Maurice Wilkins Centre for Biodiscovery, Auckland, New Zealand.

In mammals, lactation is associated with a period of infertility, characterised by reduced pulsatile luteinizing hormone (LH) secretion, cessation of ovulation and loss of kisspeptin input to GnRH neurons. However, the mechanism underlying lactational infertility is currently unclear. The anterior pituitary hormone, prolactin, named for its role in milk production, is chronically elevated during lactation and in non-lactating females, hyperprolactinaemia has been shown to lead to infertility. We aim to test the hypothesis that elevated prolactin is required for the suppression of fertility during lactation. Specifically, we aimed to investigate whether prolactin action in the brain plays a key role in suppressing kisspeptin expression and pulsatile LH secretion during lactation. Mice with a conditional deletion of the prolactin receptor in forebrain neurons (*Prlr*$^{lox/lox}$/CKC-cre), were used to test if prolactin receptor-mediated signaling in neurons is required for lactational fertility. Our preliminary data indicated that all *Prlr*$^{lox/lox}$/CKC-cre mice resume estrus cyclicity early in lactation (lactation day 5-10) compared to control *Prlr*$^{lox/lox}$ mice (does not resume until after lactation day 21). LH pulsatility was examined in virgin and lactating mice by collecting frequent blood samples from the tail tip vein over 3 hours, and LH concentrations measured by ELISA. In the lactating mice, blood sampling was conducted in the *Prlr*$^{lox/lox}$/CKC- cre mice after the resumption of estrus cyclity, with blood samples collected from control *Prlr*$^{lox/lox}$ mice on the equivalent day of lactation (during lactation diestrus). Following collection of blood samples, mice were perfused for immunohistochemistry analysis of kisspeptin cell number in the hypothalamus. We predict that resumption of LH pulsatility will be seen in the *Prlr*$^{lox/lox}$/CKC-cre, and that the lactation-induced suppression of kisspeptin will be absent allowing for the early estrus cyclicity. These results would indicate that high levels of prolactin action in the brain during lactation is crucial for maintaining lactational anovulation.

Investigating the projections of suprachiasmatic nucleus vasopressin neurons to preoptic kisspeptin neurons

Jamieson, B.B., Braine, A.K., Bouwer, G.T., Campbell, R.E., Piet, R.
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The activity of kisspeptin neurons in the rostral periventricular region of the third ventricle (RP3V) drives the surge of gonadotropin-releasing hormone that triggers ovulation. In female rodents, this preovulatory hormonal surge is dependent on circadian inputs from the suprachiasmatic nucleus (SCN). One potentially important input is that from SCN vasopressin (AVP)-expressing neurons to RP3V kisspeptin neurons. We used viral-mediated expression of a cre-dependent red fluorescent reporter to reveal the axonal projections of SCN AVP neurons to the RP3V, in mice expressing cre-recombinase in AVP-expressing neurons (AVP-IRES2-cre). Immunohistochemistry reveals a strong correlation between the level of reporter expression in the SCN and that of reporter-expressing fibres innervating the RP3V ($n = 6$, $p = 0.007$). In contrast, other AVP-expressing regions of the brain, the paraventricular and supraoptic nuclei do not appear to project to the RP3V. Quantification of the SCN AVP projections to the RP3V indicates that reporter-expressing fibres make close appositions with 54.1 ± 8.0% of kisspeptin neurons, suggesting putative synaptic inputs.
Functionally, this system was investigated by combining optogenetics and whole-cell patch-clamp electrophysiology in brain slices. AVP-IRES2-cre mice were crossed onto a mouse line expressing the green fluorescent protein in kisspeptin neurons. These were then injected with a cre-dependent blue-light sensitive protein, channelrhodopsin (ChR2). Activation of ChR2 with blue light faithfully drives action potential generation in SCN AVP neurons over 1 – 50 Hz ($n = 7$). As the SCN is predominantly a GABAergic nucleus, we examined whether blue-light activation of SCN AVP neuron projections would result in GABA release onto RP3V kisspeptin neurons. In the great majority of kisspeptin neurons (13 out of 14), however, no post-synaptic currents were recorded in response to blue-light stimulation. Thus, despite projecting to the RP3V, it appears that SCN AVP population may not communicate with kisspeptin neurons via GABA release.

The role of RFRP neurons in puberty onset and depression

India L. Sawyer, Greg M. Anderson. Centre for Neuroendocrinology and Department of Anatomy, School of Biomedical Sciences, University of Otago, Dunedin.

RF-amide related-peptide (RFRP) neurons are thought to modulate reproductive function and stress responses. Using transgenic mice which have either stimulatory or inhibitory designer-receptors exclusively activated by designer-drugs (DREADDs) selectively expressed in RFRP neurons via a Cre-loxP system, we explored the reproductive and behavioural effects of RFRP neurons non-invasively in vivo. The role of RFRP neurons in puberty onset was investigated by stimulating and inhibiting RFRP neurons through administration of the DREADD ligand clozapine-n-oxide (CNO) from post-natal days 26-31 (5mg/day orally). Stimulation of RFRP neurons in male mice led to delayed puberty onset, assessed by preputial separation (stimulated mice: 31.7±0.8 vs controls: 29.3±0.3 days old; $P<0.05$) and inhibition of RFRP neurons led to a delay in age at first successful mating (inhibited mice: 50.6±2.8 vs controls: 47.6±1.4 days old; $P<0.05$). In females, there was no difference in puberty onset. The role of RFRP neurons in stress-related behaviours was investigated in 8-week-old male mice following acute CNO administration (1 mg/kg s.c.). There were no changes in anxiety-like behaviours. There was, however, an increase in depression-like behaviour following stimulation of RFRP neurons. Stimulated mice spent more time immobilised (indicative of despair) than control mice (66.5±4.1 vs 38.4±6.9% respectively; $P<0.05$) in the last 2 minutes of a 5-min forced-swim test. These findings indicate the RFRP neurons inhibit male puberty onset, and indicate a novel role for RFRP neurons in the control of depression-like behaviour in mice. More behavioural testing will be conducted to elucidate this role. Characterizing the functions of RFRP neurons is an important step towards understanding their role and therapeutic potential in human infertility and mental illness.

Preoptic neurons are sufficient to mediate at least some of leptin's effects on fertility

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Leptin communicates information about metabolic status to the gonadotropin-releasing hormone (GnRH) neurons indirectly via afferent neuronal populations in the hypothalamus; a required relay for normal reproductive function[1]. Recent analysis of neurons located in the preoptic area of the hypothalamus suggests these may play a vital role in the rapid communication of leptin with the reproductive axis[2]. We aim to elucidate whether neurons located in the preoptic area are sufficient to mediate leptin signalling; permitting normal reproductive function in the absence of leptin signals from any other region.

Cre-loxP methodology was used to generate mice in which expression of leptin receptor (Lepr) was Cre-dependant. A proportion of these then underwent selective activation ('rescue') of Lepr only in the preoptic area. This occurred by administration of Cre DNA via an adeno-associated virus (AAV) in adulthood, enabling comparison of puberty onset and adult fertility between Lepr-rescue, Lepr-null and wild type (WT) mice (n=5-8 per group). The AAV treatment had no effect on body weight compared to obese Lepr-null mice ($p>0.05$). As expected, a significant difference was observed in the occurrence of puberty onset between WT and Lepr-null mice as only 14% of male and 0 female Lepr-null mice underwent puberty prior to 2 months of age ($P=0.002$). However, 2-4 weeks following AAV treatment, 60% of female and 100% of male Lepr-rescue had puberty compared to only 16% of female and 45% of male Lepr-null mice ($P=0.01$ and 0.19 for males and females respectively). Reproductive cycles were evident in 60% of Lepr-rescue and 0% of Lepr-null mice ($P=0.08$). Fecundity tests currently in progress.

These preliminary results suggest that preoptic neurons, at least in males, are sufficient mediators for much of the regulation of GnRH neurons by leptin. Understanding of the metabolic regulation of reproductive function will enable prevention and treatment of metabolic-associated infertility.

References

1. Quennell JH, Mulligan AC, Tups A, Liu X, Phipps SJ, Kemp CJ, Herbison AE, Grattan DR, Anderson GM (2009) *Leptin indirectly regulates gonadotropin-releasing hormone neuronal function.* Endocrinology 150:2805-2812.

2. Bellefontaine N, Chachlaki K, Parkash J, Vanacker C, Colledge W, d'Anglemont de Tassigny X, Garthwaite J, Bouret SG, Prevot V (2014*) Leptin-dependent neuronal NO signaling in the preoptic hypothalamus facilitates reproduction.* The Journal of clinical investigation 124:2550-2559.