The Case for ß-cell Preservation in Type 2 Diabetes Mellitus

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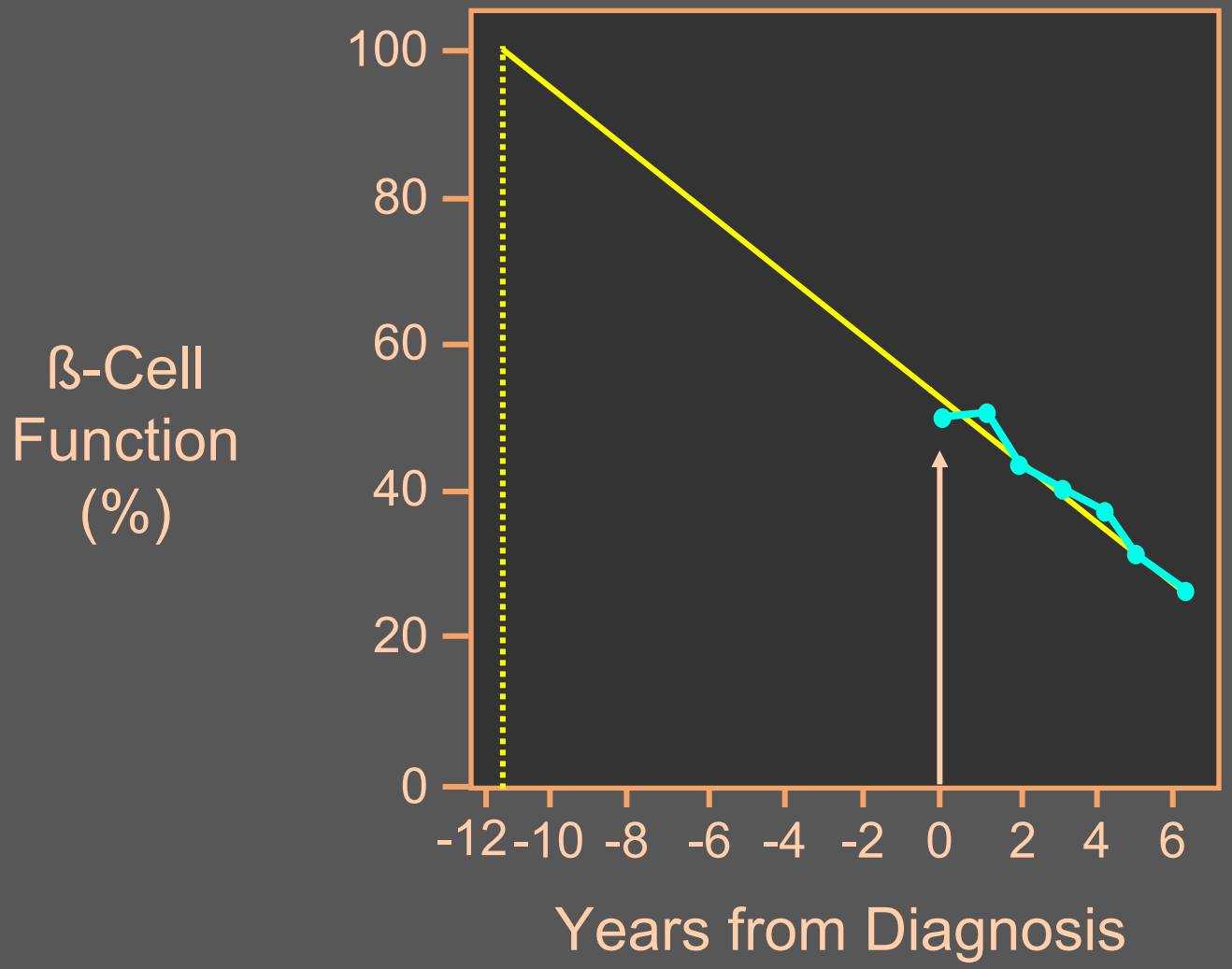
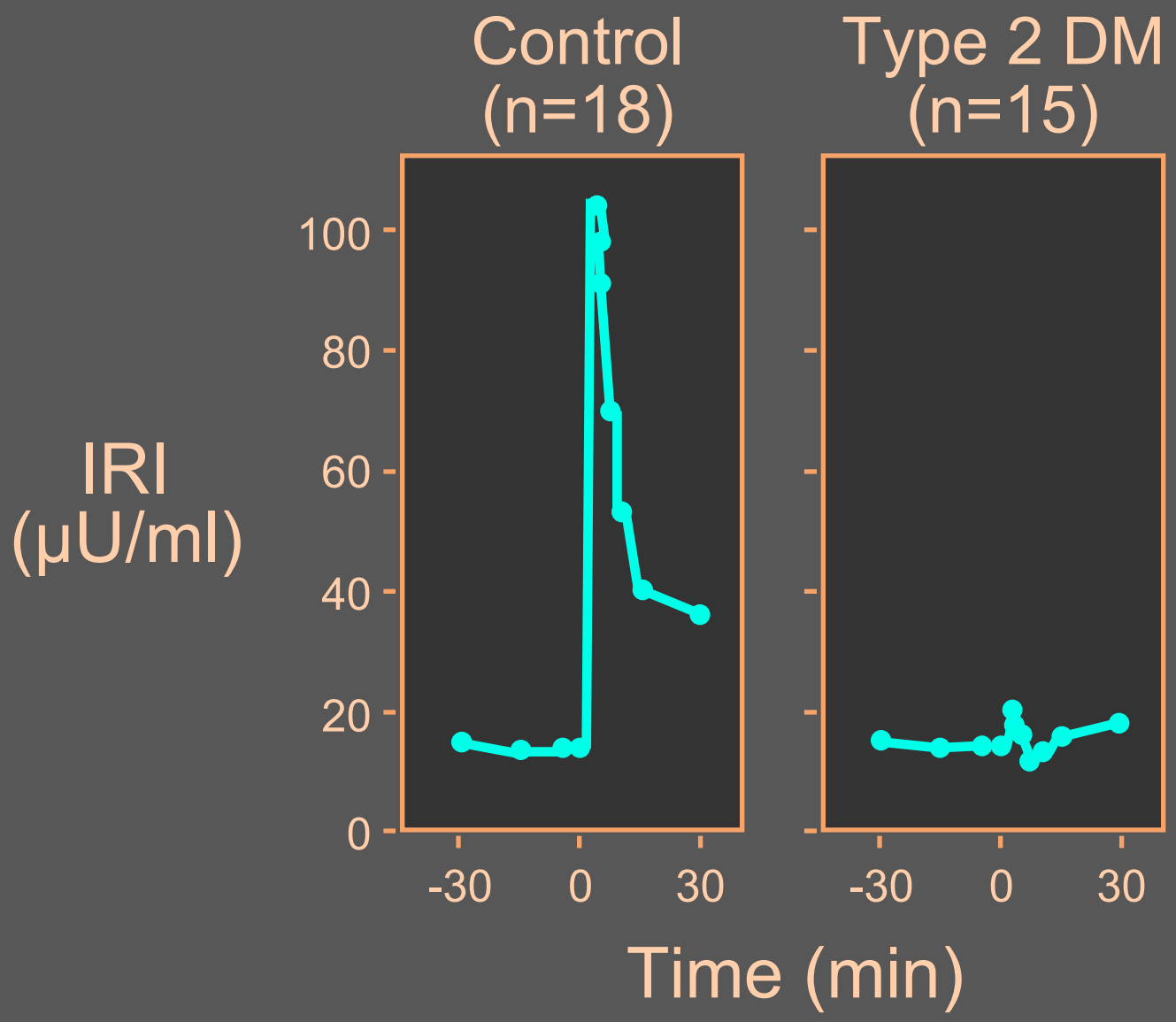
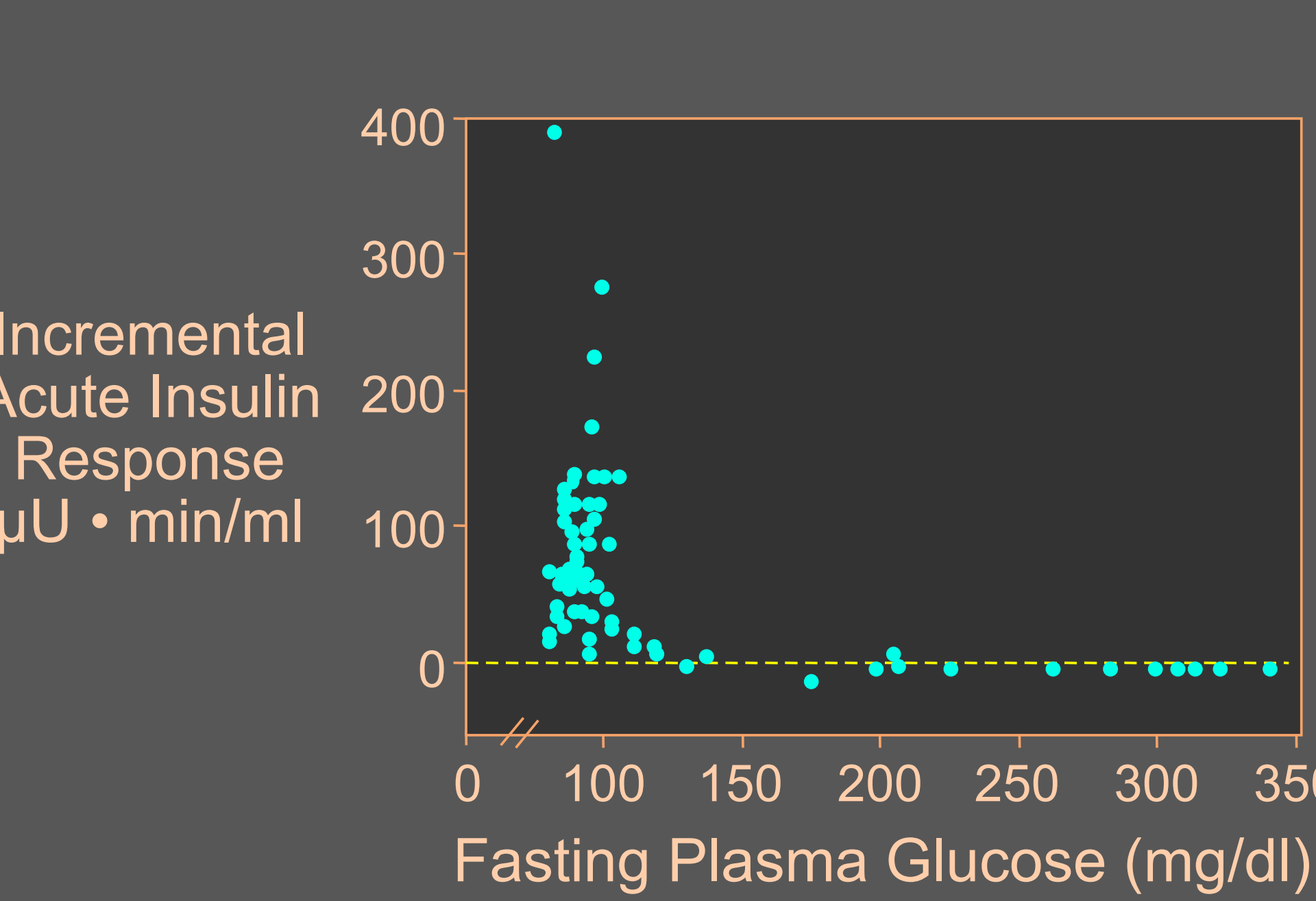
ß-cell Function in the UKPDS



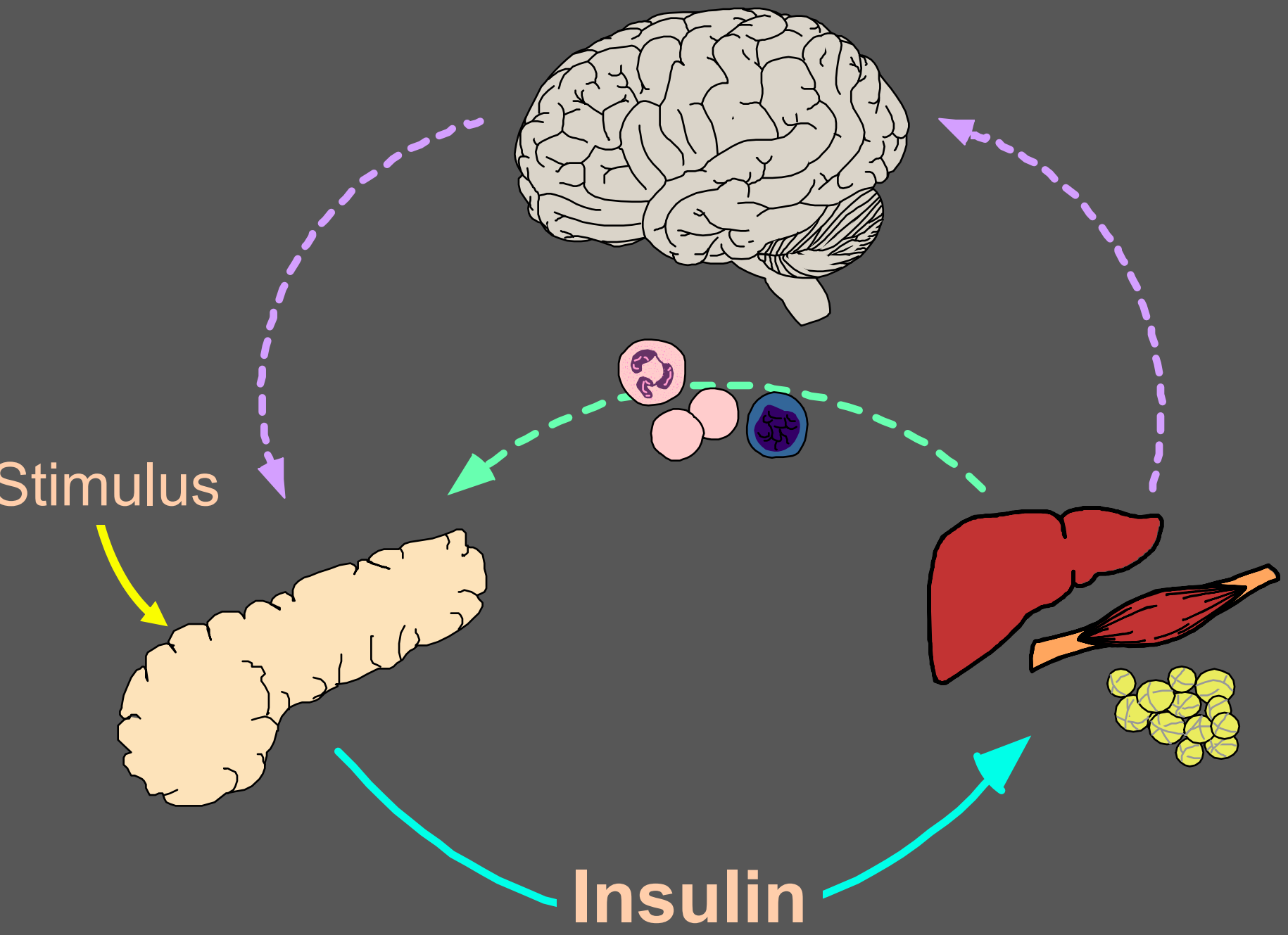
an RR. Diabetes Res Clin Pract 40 (Suppl I):S21-S25; 1998

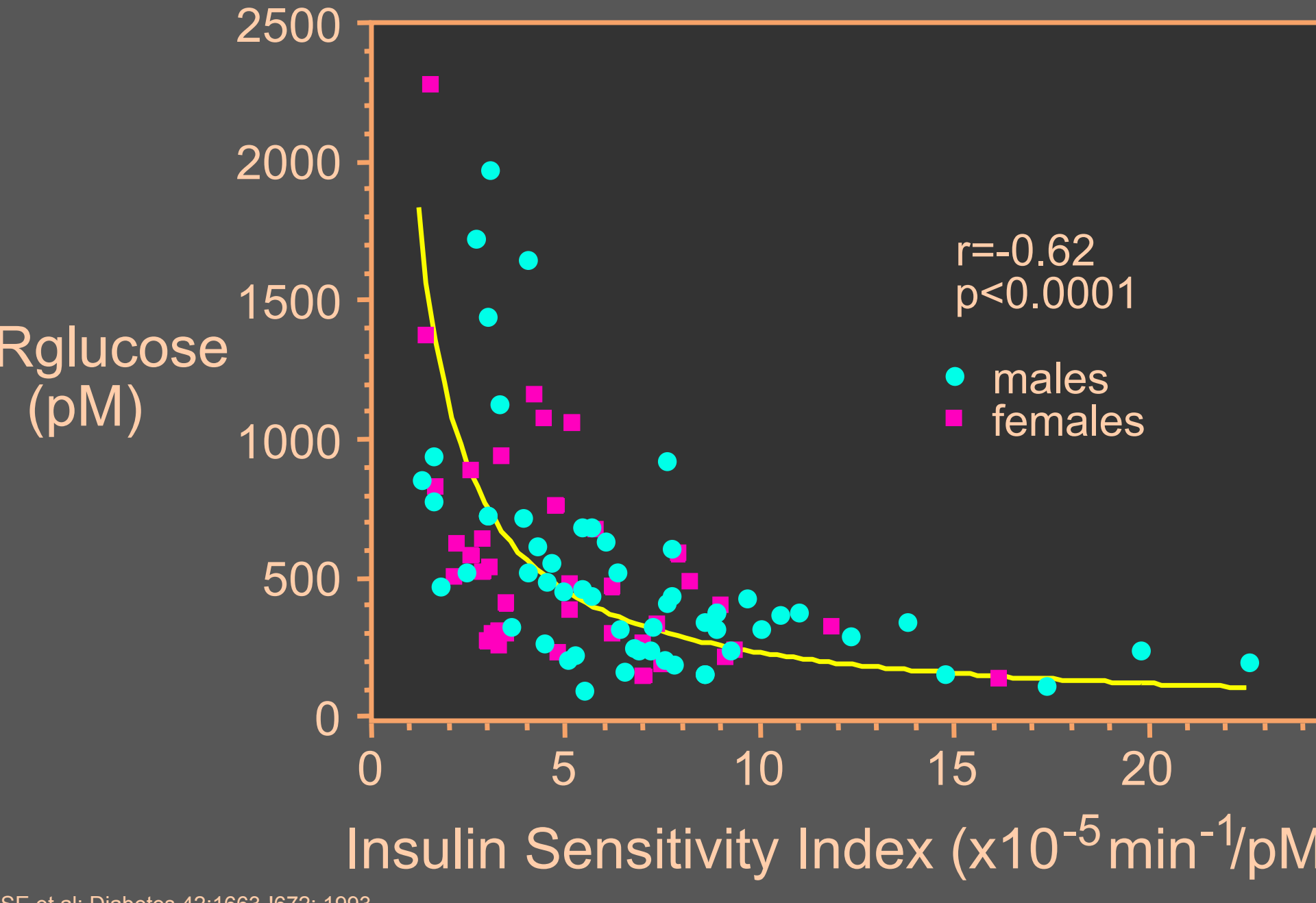
Acute Insulin Response to Glucose



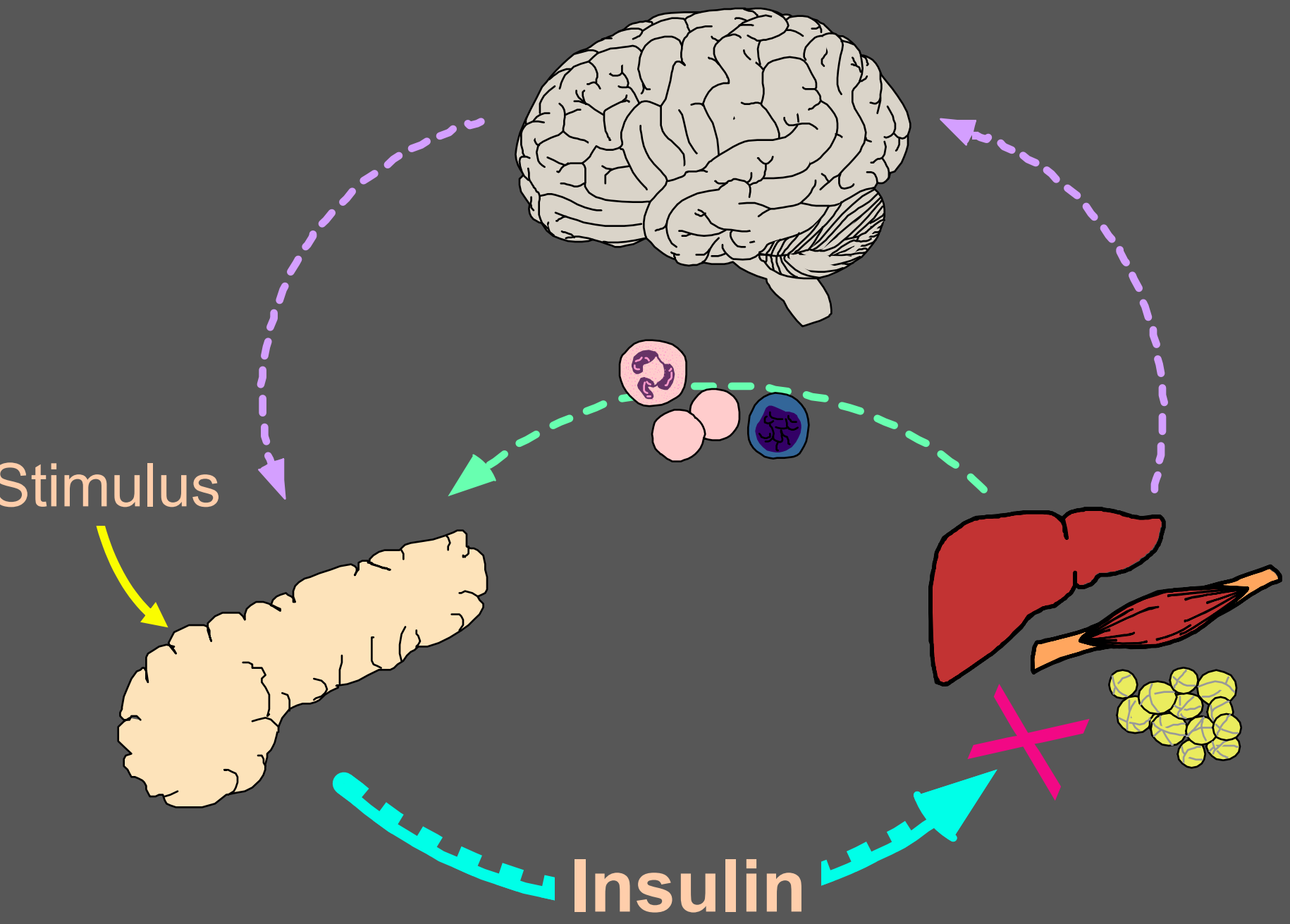


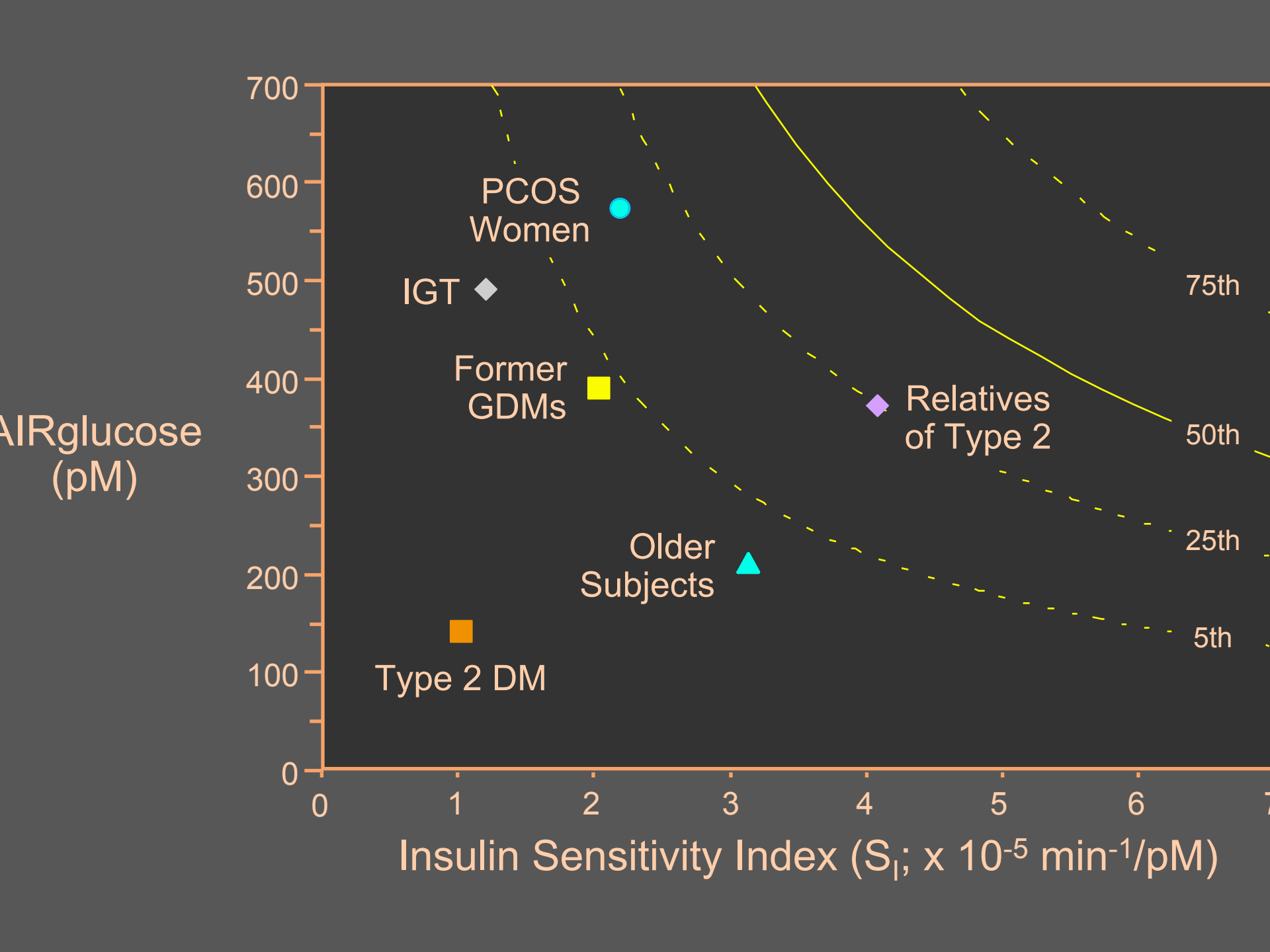
nzell JD et al: J Clin Endocrinol Metab 42:222-228; 1976


Stimulus
Insulin

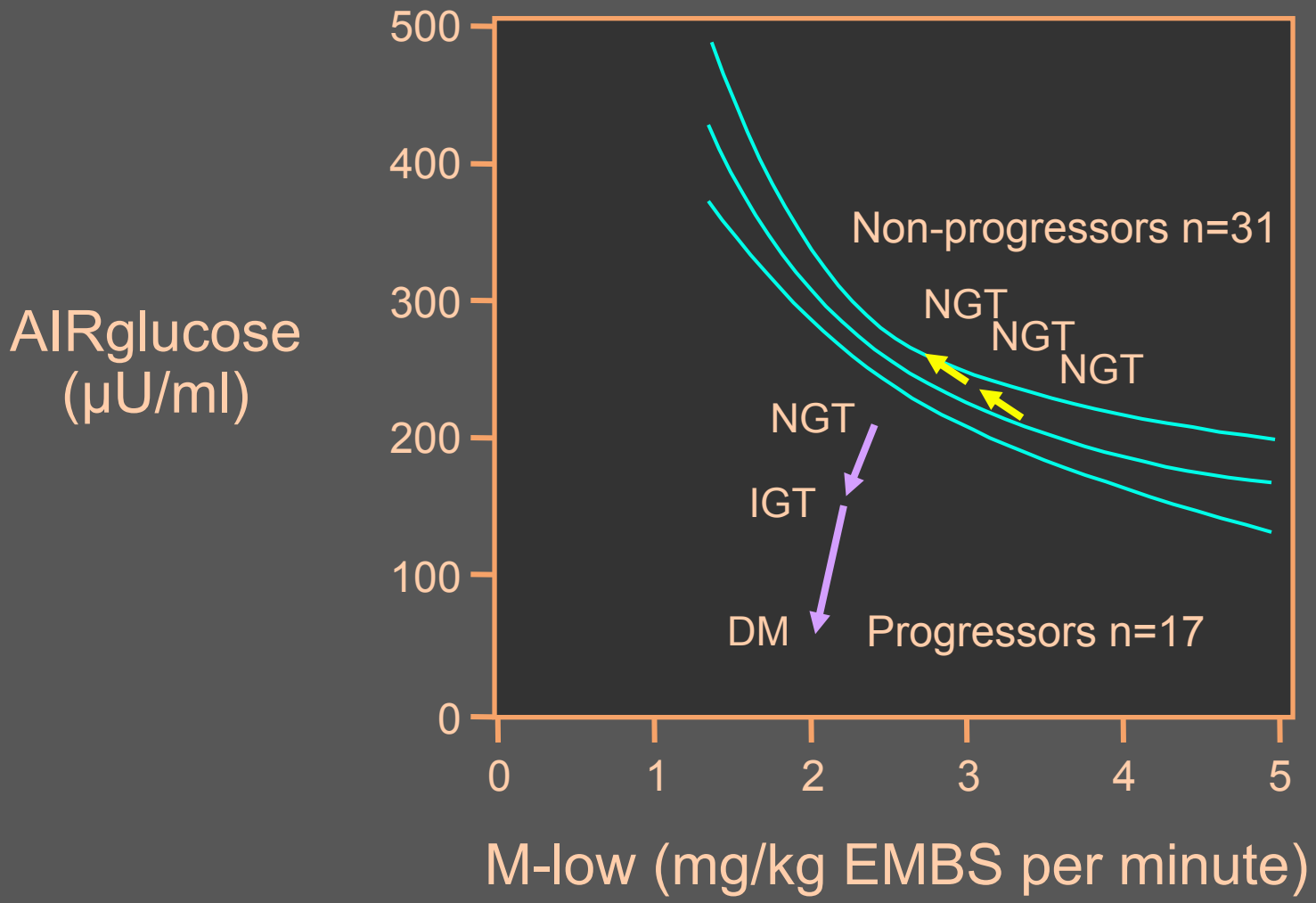


SE et al: Diabetes 42:1663-!672; 1993


Stimulus
Insulin

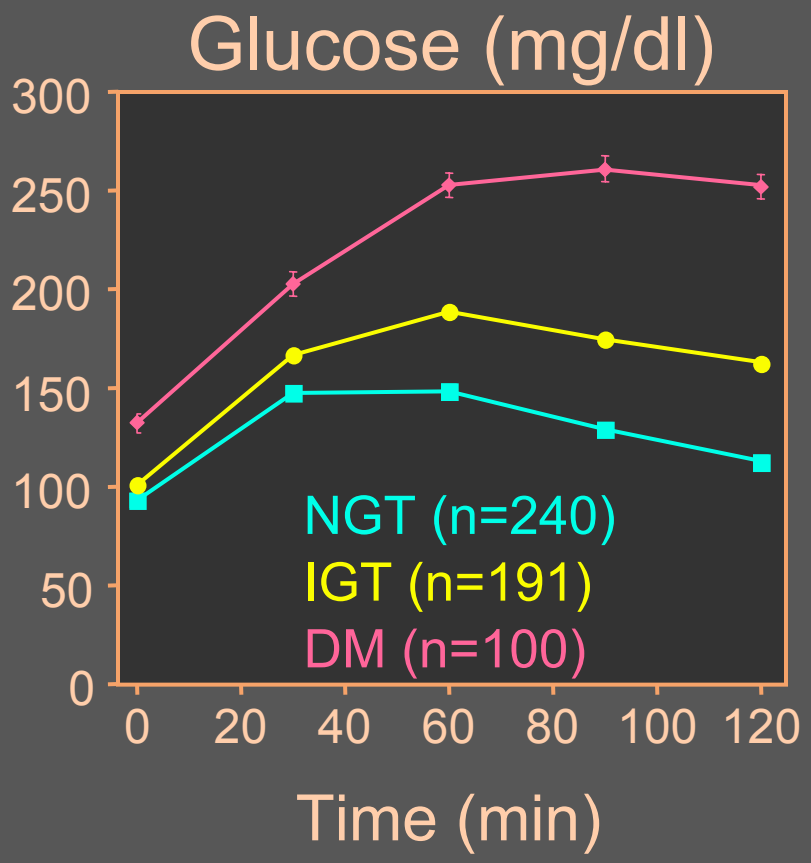

AIRglucose (pM)
700
600
500
400
300
200
100
0
0
1
2
3
4
5
6
PCOS Women
IGT
Former GDMs
Relatives of Type 2
Older Subjects
Type 2 DM
75th
50th
25th
5th
Insulin Sensitivity Index (S_I; x 10^{-5} min^{-1}/pM)

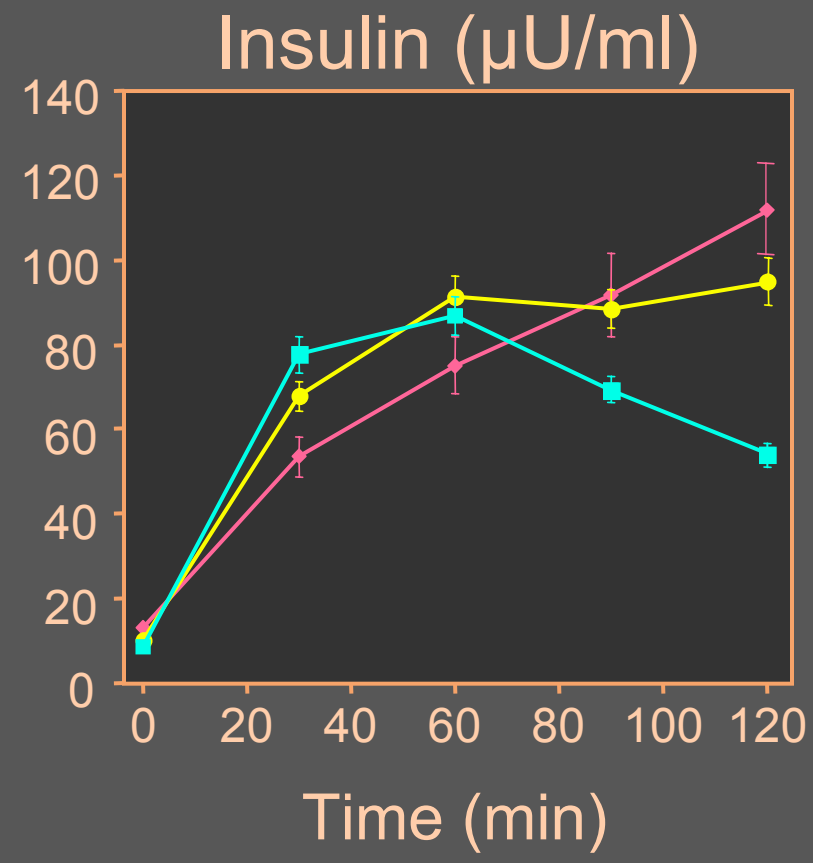
Progression to Type 2 Diabetes in Pima Indians



r C et al: J Clin Invest 104:787-794; 1999

Glucose and Insulin Responses During an OGTT in First Degree Relatives



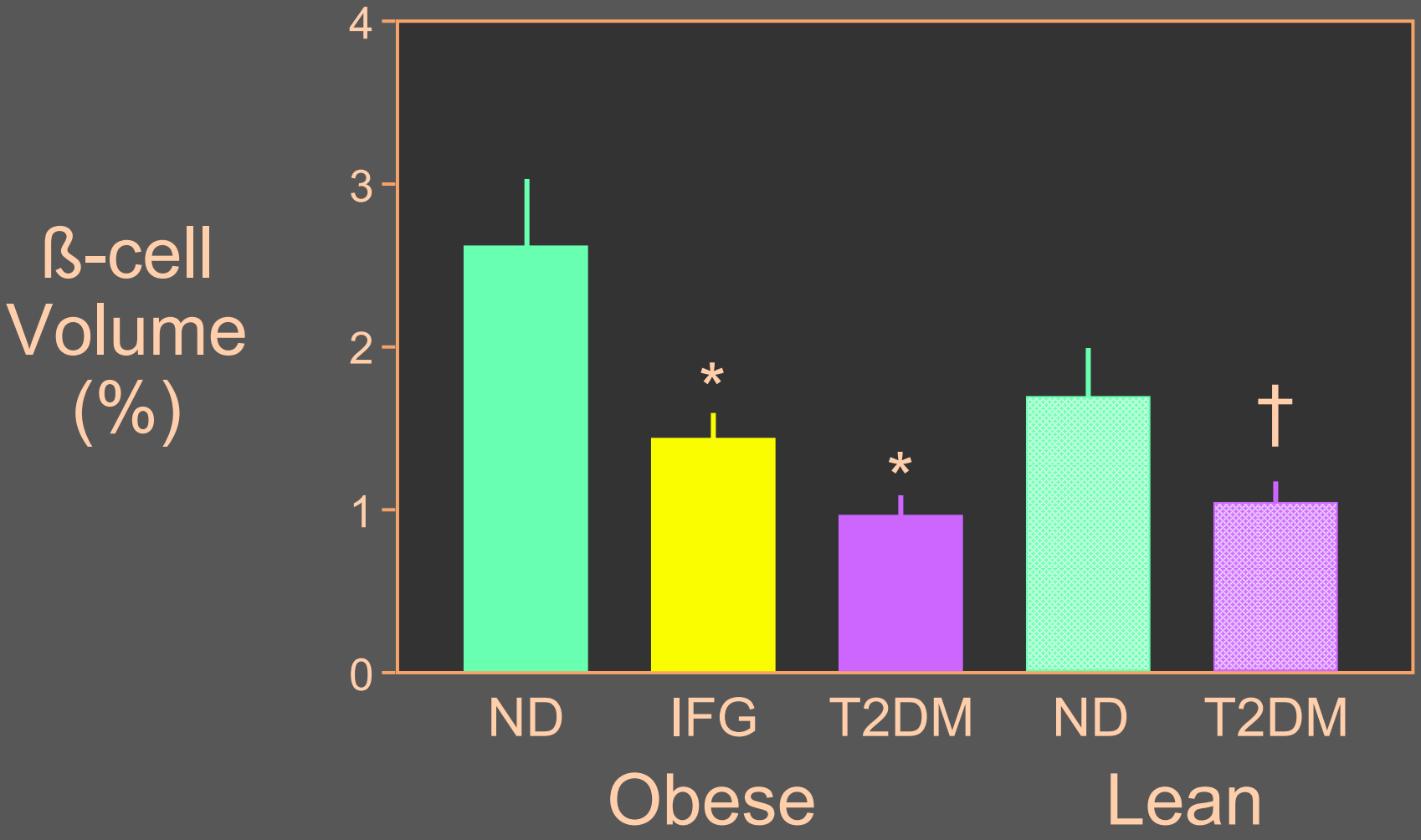


sen CC et al: Diabetes 51:2170-2178; 2002

Possible Causes of ß-cell Dysfunction in Type 2 Diabetes

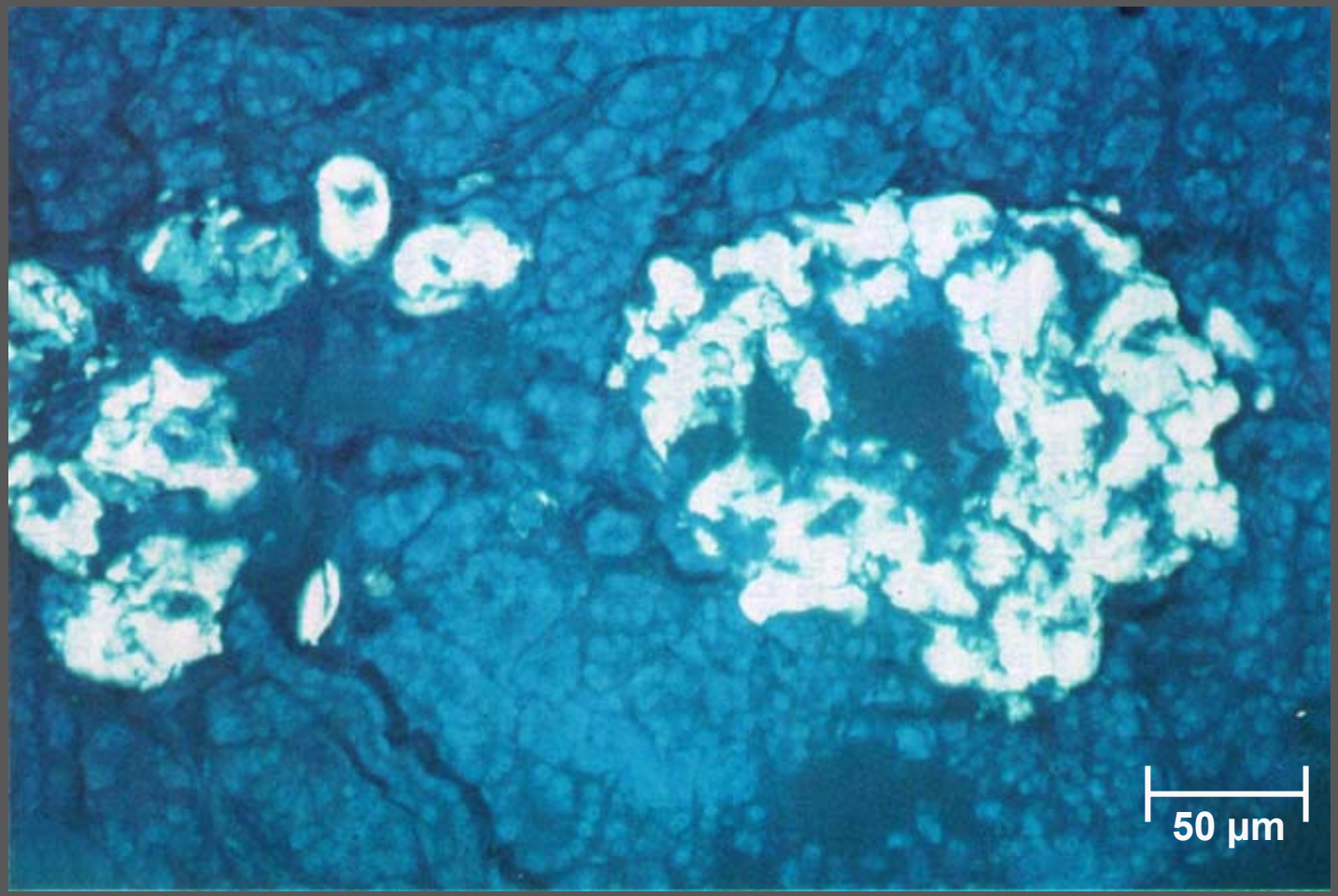
- Glucotoxicity
- Lipotoxicity
- ß-cell mass loss

ß-cell Volume is Decreased in IFG and Type 2 Diabetes



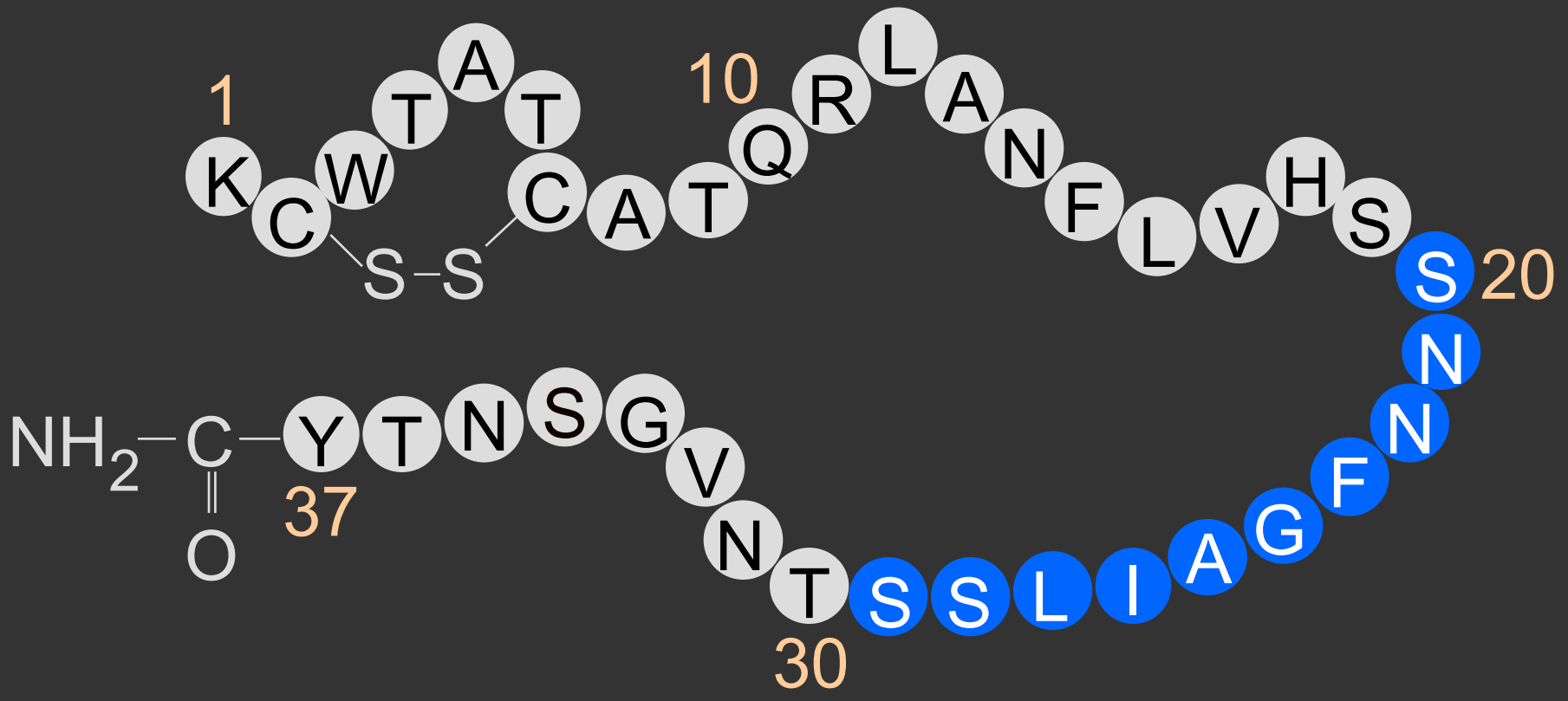
AE et al: Diabetes 52:102-110; 2003

Islet Amyloid in Type 2 Diabetes

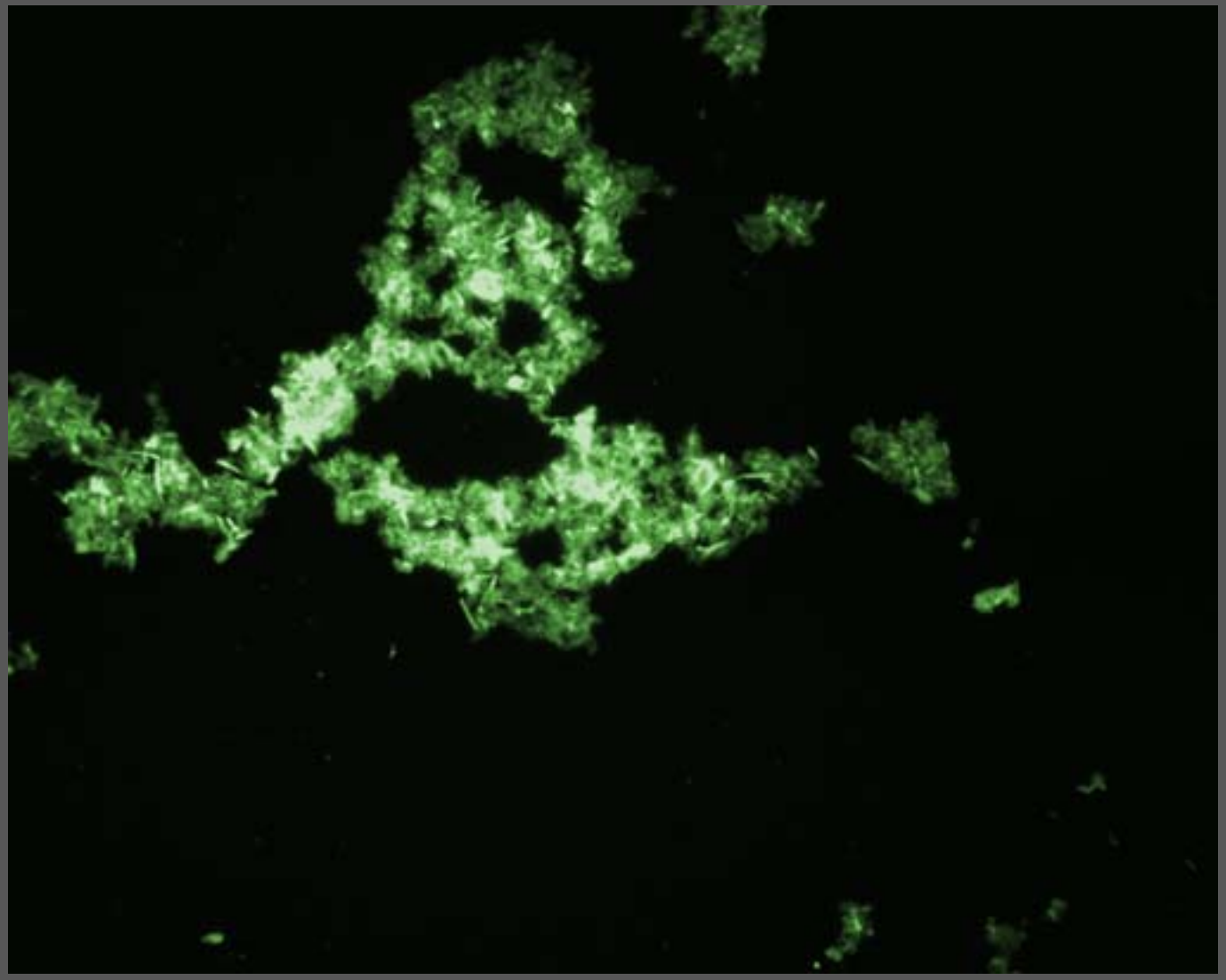


here CB et al. PNAS 93:3492-3496; 1996

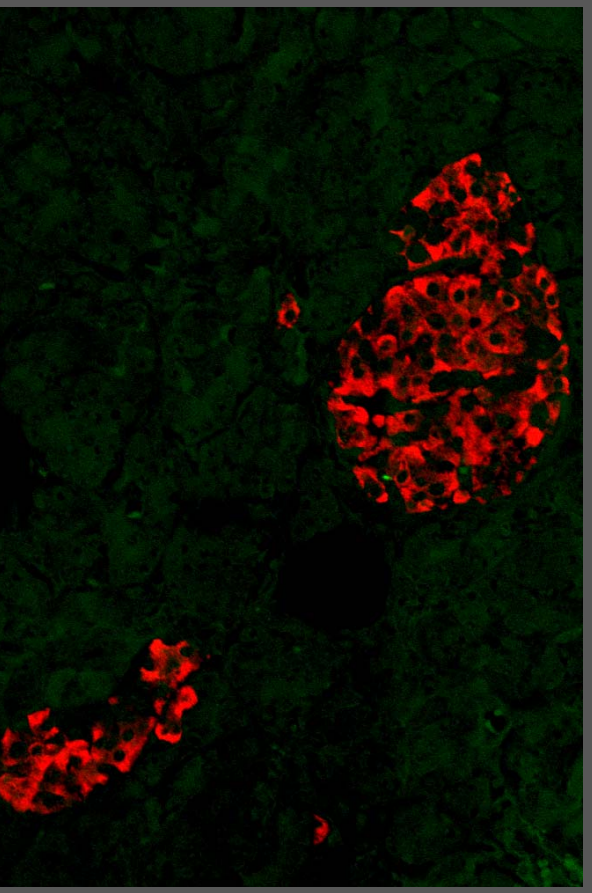
Islet Amyloid Polypeptide/Amylin

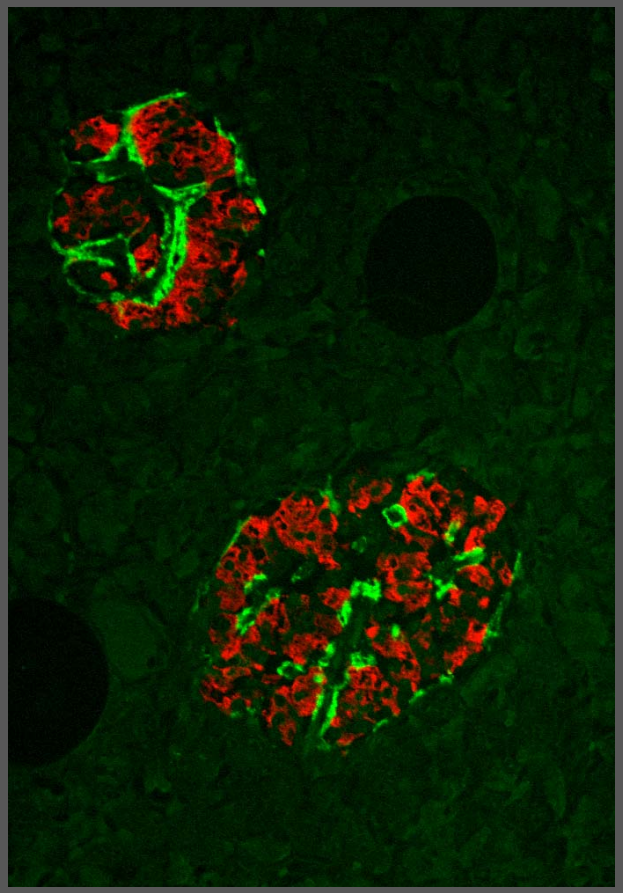


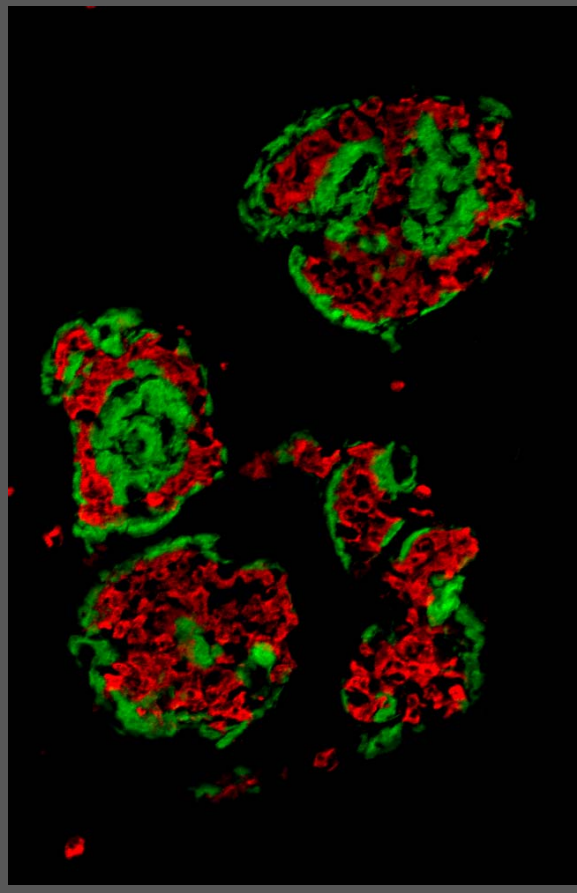
hioflavin S Staining of Human IAPP Fibril



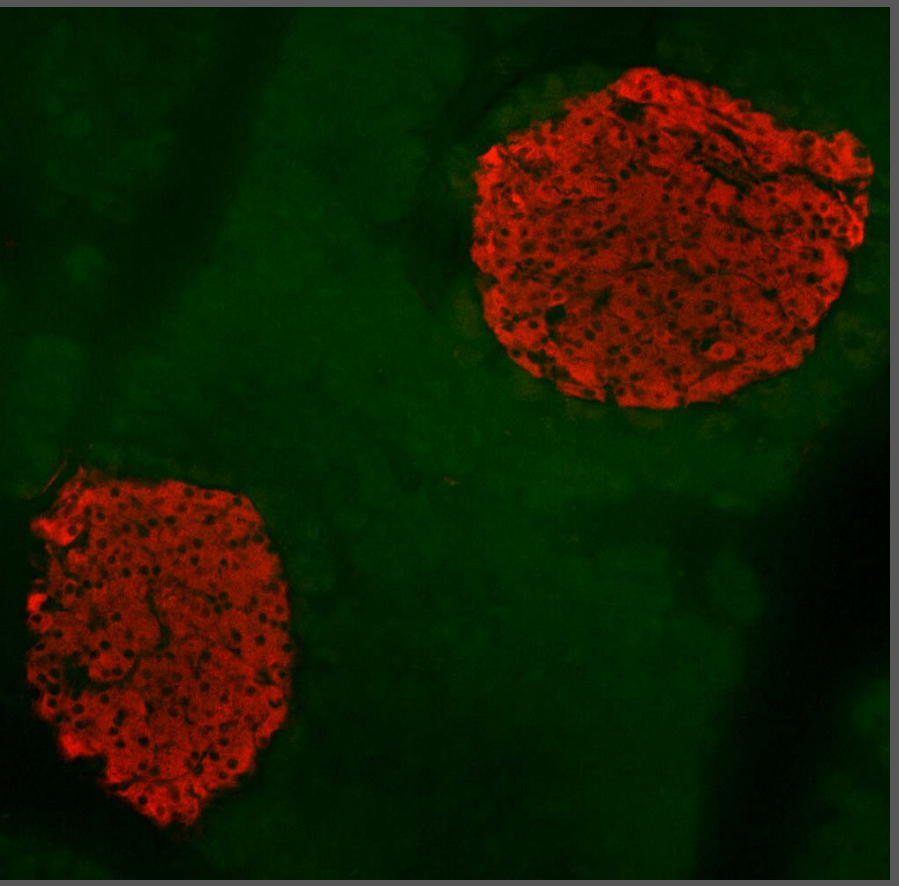
Human Islets



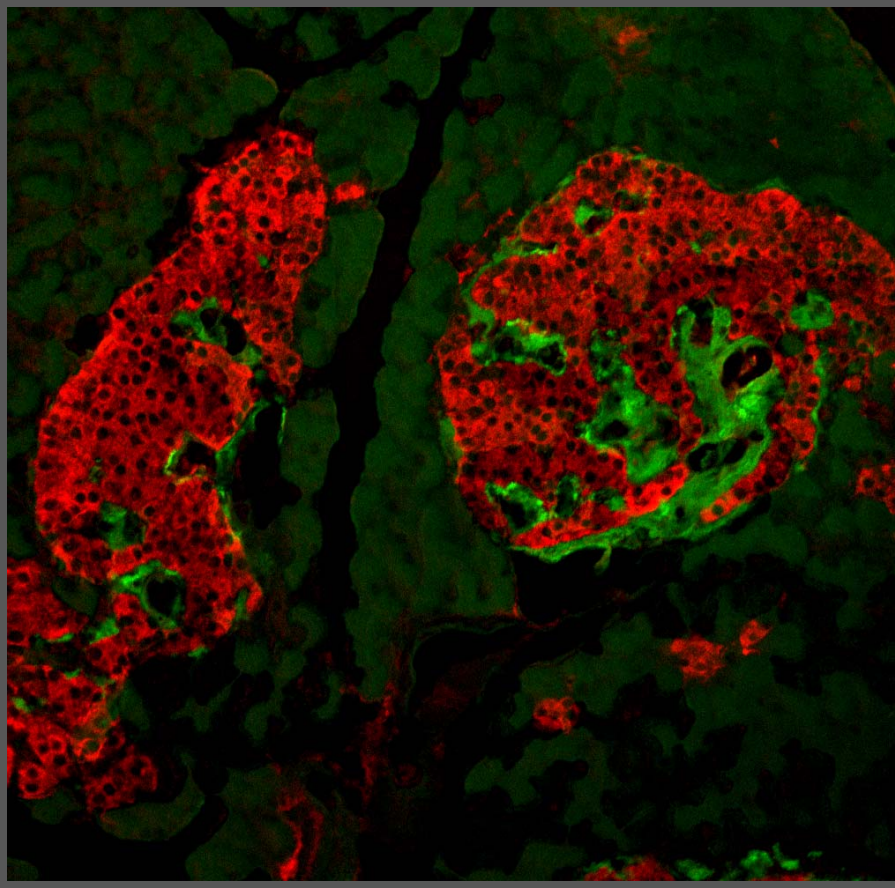




Mouse Islets



Non-transgenic



hIAPP Transgenic

In a human IAPP transgenic mouse model of islet amyloid in vivo:

1. amyloid deposition occurs diffusely involving nearly all islets before becoming severe and replacing ß-cells;

2. increased dietary fat increases amyloid deposition; and

3. apoE is not critical.