and identity. Evidence from in vitro studies demonstrated that human embryonic stem cells depend on basic fibroblast growth factor (bFGF) signaling. bFGF stimulates fibroblast-like support cells to produce insulin-like growth factor-2 (IGF-2), a factor sufficient to maintain human embryonic stem cell cultures (7). Similarly, neonatal spermatogonial stem cell pluripotency is maintained by the secretion of IGF-1 by Leydig support cells in vitro (8). In the mouse small intestine, IGF-1 is expressed in the subepithelial muscle cells (9), suggesting that mammalian intestinal growth may be regulated by a mechanism similar to that observed in Drosophila.

Vertebrate niche cells can relay a variety of stimuli through the insulin signaling cascade. Cone photoreceptor cells in the teleost retina produce IGF-1 in a time-of-day–dependent cycle. Application of IGF-1 increases the proliferation of rod progenitor cells in vivo, with the greatest sensitivity at night, coinciding with peak endogenous IGF-1 expression. Conversely, blocking the IGF-1 receptor, which is expressed on the rod progenitor cells, decreases their proliferation (10). Thus, localized insulin signaling can be controlled by nonmetabolic stimuli and may contribute to progenitor cell response to diverse external stimuli.

Local insulin also plays a role in mediating the proliferation of progenitor cells in response to tissue damage. In rats, induction of focal ischemia causes neuronal cell death. After ischemia, brain astrocytes (a type of glial cell) near the damaged area produce IGF-1, promoting proliferation of neighboring neural progenitors in the dentate gyrus of the adult rat hippocampus (11). Forced expression of IGF-1 in astrocytes promotes localized overgrowth of the brain in rodents (11), whereas direct infusion of IGF-1 into specific brain regions can induce neurogenesis in healthy adult mammalian brains (12). This parallels the role of glial-derived insulin in increasing neural stem cell proliferation in Drosophila (4, 5). Other stimuli, including exercise, also promote neurogenesis in the proliferative subventricular zone and dentate gyrus regions of the adult mouse brain, although this appears to be through systemic IGF-1 signaling (13, 14).

The discovery that stem cells are sensitive to locally produced insulin could open new avenues in the use of IGFs to activate particular stem cell populations after tissue damage or disease. The cerebrospinal fluid provides access for cerebral cortical progenitor cells in the mouse brain to insulin-like peptides (15). Infusion of insulin-like peptides into this fluid or into particular brain regions may allow moderation of the effects of injury or neurodegeneration.

Differences in local versus systemic signaling under caloric restriction may favor the maintenance rather than proliferation of stem cell pools. This may help to explain the apparent contradiction that, although reduced insulin signaling increases life span in mammals and invertebrates, insulin signaling has a neuroprotective effect in the central nervous system (16).

Several key questions are yet to be answered about local insulin signaling, including how systemic signals are functionally coupled to niche insulin signals, how different niche signals integrate to control stem cell behavior, and how local insulin signaling changes in aging and disease. Understanding these interactions will enable a greater understanding of stem cell dynamics in response to external signals and metabolic state.
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rted such that there is a net piezo-	ricit on Si by devitrification of amorphous mesoporous silica films (1).
ly simple but mechanistically complex:
films are prepared by dip-coating from alco-
ly straightforward and yet quite complex:
rsor or large or small mesopores. Doping with Sr(NO3)2 or Ba(OH)2 is ac-
mplished either in situ or in a secondary step. Heat treatment in air to 900°C to 1000°C results in
highly oriented α-quartz on silicon (see the
ure, panel B).
known crystalline, the α-quartz film bears an epitaxial relationship with the
underlying (100) face of the Si substrate (see the figure, panel C), and the columnar
ystals are oriented such that there is a net piezo-
elactic effect. In comparison, randomly ori-
ented or multivariant crystallites would show
net piezoelectricity, requiring thermal gra-
dients achieved by rapid thermal processing
) or deposition of seed layers (8) to direct
orientated crystal growth.

The use of chemical, stress, and electric
field gradients have also been developed as
a polar variant-selective or self-polarization
mechanism for LiNbO3 and several other
piezoelectric films and crystals (9). The
dimensional scale of the oriented cylindrical
porosity formed in the amorphous silica
precursor films is more or less preserved for
macroporous and large mesoporous speci-
men after crystallization, resulting in opti-
cally transparent, piezoelectric quartz thin
films composed of oriented arrays of
mesopores (around 3 nm diameter) devitrify
form dense epitaxial α-quartz films.

The detailed mechanism of the devitrifica-
crystallization process is presently under
study, but it is sensitive to Sr or Ba, which,
along with the OH content inherent to high-
surface-area solution-derived amorphous
silica (10), promote devitrification (11). For
macroporous and large mesoporous films,
devitrification is confined within the pore
walls. The columnar nanoscale crystallites
suggest that quartz is nucleated at the SiO2/
Si interface, where, through a heteroepitaxial
relationship with Si(100), α-quartz is selected for.
As crystallization proceeds from the
urface by competitive growth of properly ori-
ented crystallites, Sr or Ba as well as OH are
cluded at the growth front, or conceivably
ce the pore walls, and transported to the fi
surface leaving no trace of Sr or Ba within the
film or at the Si interface.

The film porosity and nanoscale dimen-
sions of the silica pores and walls appear key to
the growth mechanism. First, below a wall
ickness of several nanometers, crystalliza-
tion consumes the parent film to form an ori-
ented dense α-quartz film, suggesting that
the silica pore wall needs to be thicker than
a critical nucleus size (or that the pore curva-
ture be less than a critical value) to support
confined/templated devitrification. Second, the
transformation from amorphous silica to
α-quartz is accompanied by a substantial den-
sity increase from ~2.0 g/cm³ to ~2.65 g/cm³;
the thinness and weak lateral constraint of the
pore wall may allow this devitrification strain
to be accommodated by shrinkage of the walls
as opposed to film thickness (shrinkage par-
allel to the substrate is precluded by coher-
ency of the quartz/Si interface). The influence
do differential strain is further evident from
crystallographically oriented euhedral/fac-
eted domains that are mechanically detached
along their peripheries allowing localized
two-dimensional shrinkage and stress release.

The work by Carretero-Genervier et al.
represents one of the first examples of con-
fined, heteroepitaxial devitrification to form
an oriented polycrystalline film. Confined
devitrification of monosized amorphous silica
carbonaceous forms to form monosized α-quartz
by hydrothermal treatment in saline solutions at
200°C has been recently demonstrated (12).
Whether hydrothermal processing in NaCl- or
Sr²⁺- or Ba²⁺-containing solutions could trans-
form macro- or mesoporous silica films to
porous α-quartz remains to be seen, but such
a treatment would reduce both the process-
ing temperature and the concurrent oxidation
of the Si substrate. Additionally, lithographic
patterning and ink-jet printing of mesopo-
rous silica films on Si have been reported (5,
13), and it would be of interest to demonstrate
the patterned formation of porous piezoelec-
tric quartz. Finally, detailed measurements
of the piezoelectric properties of these films
are needed (14). Due to their polycrystal-
line nature and crystallographic alignment
directed by the substrate, we might expect
quality factors to be inferior to those of sin-
gle-crystal quartz slabs cut along preferred
statigraphic angles (15). However, the
coherent Si/quartz interface and film thinness
combined with controlled porosity may pro-
vide advanced functionality and operational
frequency range of potential interest in acous-
tic wave-based sensing and microelectrome-
chanical systems.

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